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13. ABSTRACT ***(Maximum 200 Words)***

Estradiol and related compounds bind as ligands to the estrogen receptor initiating biological reactions, which can cause either initiation/progress or inhibition of tumor growth. Slight structural variations in these molecules can change their carcinostatic potentials from agonistic to inhibitory. The principal objective of this proposal is to relate known biological reactions to physical properties such as point charges of atoms and the electrostatic potential.

We are obtaining information about these electronic properties of estrogen derivatives from experimental determination of their electron density using high quality single crystal X-ray crystallography. With the completion of the first electron density experiment of an estradiol derivative, we have proven, that the technique will indeed work for molecules of this magnitude. We have determined the electrostatic potential and related properties for estrone. Further data sets of 17α-estradiol•1/2 H_2O and 17β-estradiol•1/2 MeOH have been collected and are under investigation. Comparison of electronic properties of several estrogen derivatives is essential in order to identify certain regions of the electrostatic potential of a ligand that can be related to biological functionality. Furthermore, we solved the X-ray structures of three new crystal modifications of estradiol derivatives, which add to the overall knowledge about estradiols.

14. SUBJECT TERMS
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Table of Contents

Introduction

The principal objective of this proposal is to obtain physico-chemical information on estrogen derivatives and correlate this knowledge to their known biological functionality. Slight chemical variation in these molecules can change the carcinostatic potentials from agonistic to inhibitory. Relating these biological reactions to physical properties such as point charges of atoms and the electrostatic potential is a logical first step in the intelligent design of therapeutical drugs. We are obtaining information about the electronic properties of estrogen derivatives from experimental determination of their electron density using high quality single crystal X-ray crystallography.

Body

Task 1. Preliminary Studies on a series of crystals of estrogen derivatives

- Feasibility study of already available crystals of estrogen derivatives

  Feasibility studies on crystals of estrogen derivatives of 2-hydroxyestratrien-17β-ol, 4-hydroxyestratrien-17β-ol and 17α-estradiol demonstrated their unsuitability for charge density studies. These studies require high quality crystals of at least 0.15 mm^3. The crystals under examination proved to be either too small or not of a high enough quality.

- Development of crystallization methods for the derivatives not yet available as high quality single crystals

  We have developed crystallization methods for obtaining high quality crystals of several different estrogen derivatives. So far we succeeded in the syntheses of high quality crystals of
  - 17α-estradiol•1/2 H_2O
  - (16α)estriol
  - 17β-estradiol•urea
  - 17β-estradiol•1/2 MeOH
  - 17β-estradiol•2/3 MeOH•1/3 H_2O
  - estrone.

- Variable Temperature studies on each sample to define the appropriate temperature for the measurement

  Variable temperature studies were performed on the diffractometer on all of the above-mentioned crystals. As our criterion for stability we chose the change in mosaicity of the respective crystal as identified by the broadening of the profiles of the diffraction intensities in comparison to a room temperature measurement.

In our in-house experiments using Ag-radiation (0.56083 Å), all of the samples proved to be stable under nitrogen cooling to 100 K.

As an extension of our collaborative work with Dr. Leif Hanson (study on protein stability with He-cooling) further studies with liquid helium (ca. 17 K) were performed with synchroton radiation at the Argonnne (1.0000 Å) and Brookhaven (0.643 Å) National Laboratories Surprisingly, these studies showed deviating results: while investigations on estrone at Argonne National Laboratories proved its suitability for He-temperature charge density studies, crystals of 17α-estradiol•1/2 H_2O, 17β-estradiol•urea, 17β-estradiol•1/2 MeOH 17β-estradiol•2/3 MeOH•1/3 H_2O and estrone, studied at Brookhaven National Lab showed a vast increase in their mosaicity after cooling. Extending the time period during which a crystal was cooled to the final temperature of ca. 17 K prove to be successful for a crystal of (16α)estriol.

Importantly, these experiments have shown a vast increase of scattering power of the respective crystal at He-temperature compared to the room temperature diffraction experiment. A typical example is shown in Appendix A; the two pictures compare the scattering ability of the same crystal of 17α-estradiol•1/2 H_2O at room temperature and at 17 K. Clearly, the quality of the data is vastly superior at ca. 17 K.

We are continuing our investigations of the correlation between final temperature of the crystal, speed of cooling, flux of the beam, wavelength etc. and the mosaicity of the diffracted beam in order to enhance the crystal stability of the respective estrogen derivative.

- Routine X-ray crystal structure determination on previously uncharacterized derivatives

In the course of our crystallization efforts we crystallized and determined three new crystal modifications of estradiol derivatives:

- 17α-estradiol•1/2 H_2O (Appendix B)
- 17β-estradiol•2/3 MeOH•1/3 H_2O (Appendix C)
- 17β-estradiol•1/2MeOH (Appendix D, ref. 1)

Task2. Electron density studies on the above mentioned estrogen analogues

- Electron density studies at nitrogen temperatures on crystals that did not qualify for lower temperatures

We have collected complete high quality data sets for charge density analyses on crystals of

- 17α-estradiol•1/2 H_2O
- 17β-estradiol•1/2 MeOH
- estrone

- Electron density studies at helium temperatures

  He-temperature studies have shown unexpected instability of the estrogen derivatives (s.a.) under extreme cooling. We hope to develop cooling techniques that improve the stability of the crystals and therefore enable us to use the demonstrated vast increase in scattering power (Appendix A) for our electron density data sets.

- Analysis of the experimental data, preparation of manuscripts

  - Estrone: An electron density study including the determination of resulting electronic properties has been completed. The results were/will be presented at the Annual Meeting of the American Crystallographic Association at St. Paul, MN July 2000 (ref. 2) and the Annual European Crystallographic Meeting in Nancy, France August 2000 (ref. 3) (Appendix E). A manuscript for publication is in preparation.

  - 17α-estradiol•1/2 H_2O: The analysis of the electron density data is currently under investigation. We are preparing a manuscript describing the routine crystal structure of 17α-estradiol•1/2 H_2O (Appendix B).

  - 17β-estradiol•1/2 MeOH: Analyzing the electron density data has proven to be difficult, because the compound crystallizes in the space group P1 with four crystallographic independent estradiol molecules in the asymmetric unit. The number of parameters therefore quadruples compared to crystal structures with only one estrogen molecule in the asymmetric unit. We believe that the results of electron density determinations on similar derivatives will provide us with valuable starting values to further model the electronic properties of the crystal under investigation. A short note of the routine crystal structure of 17β-estradiol•1/2 MeOH has been published (ref. 1, Appendix D)

Key Research Accomplishments

- Crystallization of high quality crystals
- Determination of electrostatic potential and other properties of estrone
- Determination of three new crystal modifications of 17α/17β estradiols derivatives
- Methodology development for electron density experiments

Reportable Outcomes

1. Annual Meeting of the American Crystallographic Association at St. Paul, MN; July 2000 (Appendix E)
2. Annual European Crystallographic Meeting in Nancy, France; August 2000 (Appendix E)
3. D. Parrish, A. Pinkerton - *Acta Cryst. 1999* C55 (Appendix B)
4. Pre-doctoral Traineeship Award granted by the Department of the Army for Damon Parrish. $66,000 "*Measurement of the Electron Density Distribution of Estrogens - a First Step to Advanced Drug Design*"

Conclusion

With the completion of the first electron density experiment of an estradiol derivative, we have clearly demonstrated, that studies of this magnitude are indeed possible. We determined electrostatic potential and related properties for one of the three known crystal modifications of estrone. Variable temperature experiments with crystals of estrogen derivatives have revealed a beneficial enormous increase in scattering power concomitant with a broadening of the peak profile under He temperature. While our research will greatly benefit from the improved scattering power of the crystals, we have to investigate different cooling techniques to enhance the crystal stability of the respective estrogen derivative.

References

1. D. Parrish, A. Pinkerton - *Acta Cryst.* ***1999*** C55

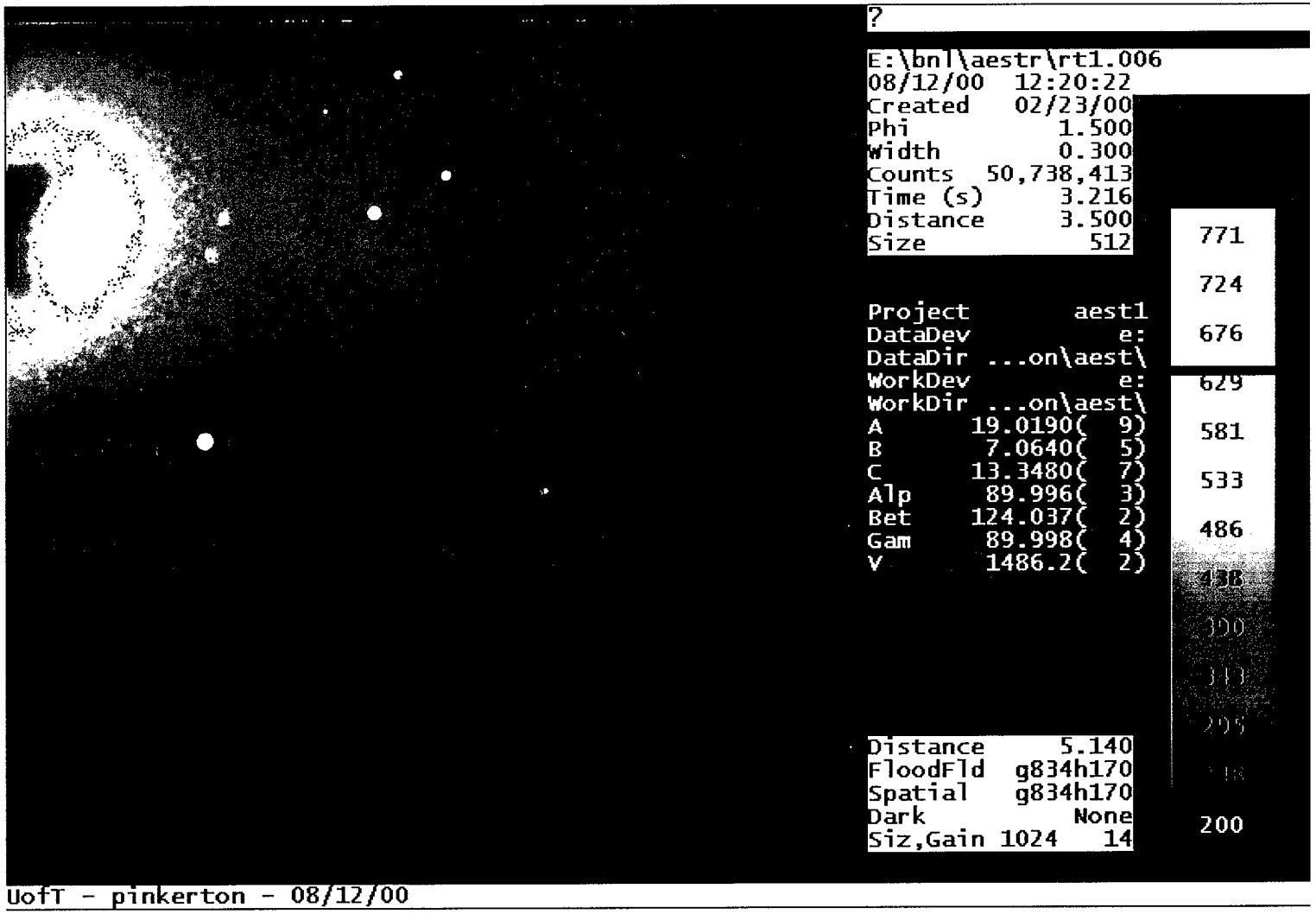
2. Damon Parrish, Nan Wu, Elizabeth Zhurova, A. Alan Pinkerton " Charge density study of estrone", Annual Meeting of the American Crystallographic Association at St. Paul, MN; July 2000 (Appendix E)

3. Damon Parrish, Nan Wu, Elizabeth Zhurova, A. Alan Pinkerton " Charge density study of estrone"; Annual European Crystallographic Meeting in Nancy, France; August 2000 (Appendix E)

Appendix A

Figure 1: Scattering of a crystal of 17α-estradiol•1/2 H_2O at room temperature

Figure 2: Scattering of the same crystal of 17α-estradiol•1/2 H_2O at He-temperature (ca. 17 K)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C 13.3480(7)
Alp 89.996(3)
Bet 124.037(2)
Gam 89.998(4)
V 1486.2(2)
Distance 5.140
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Spatial g834h170
Dark None
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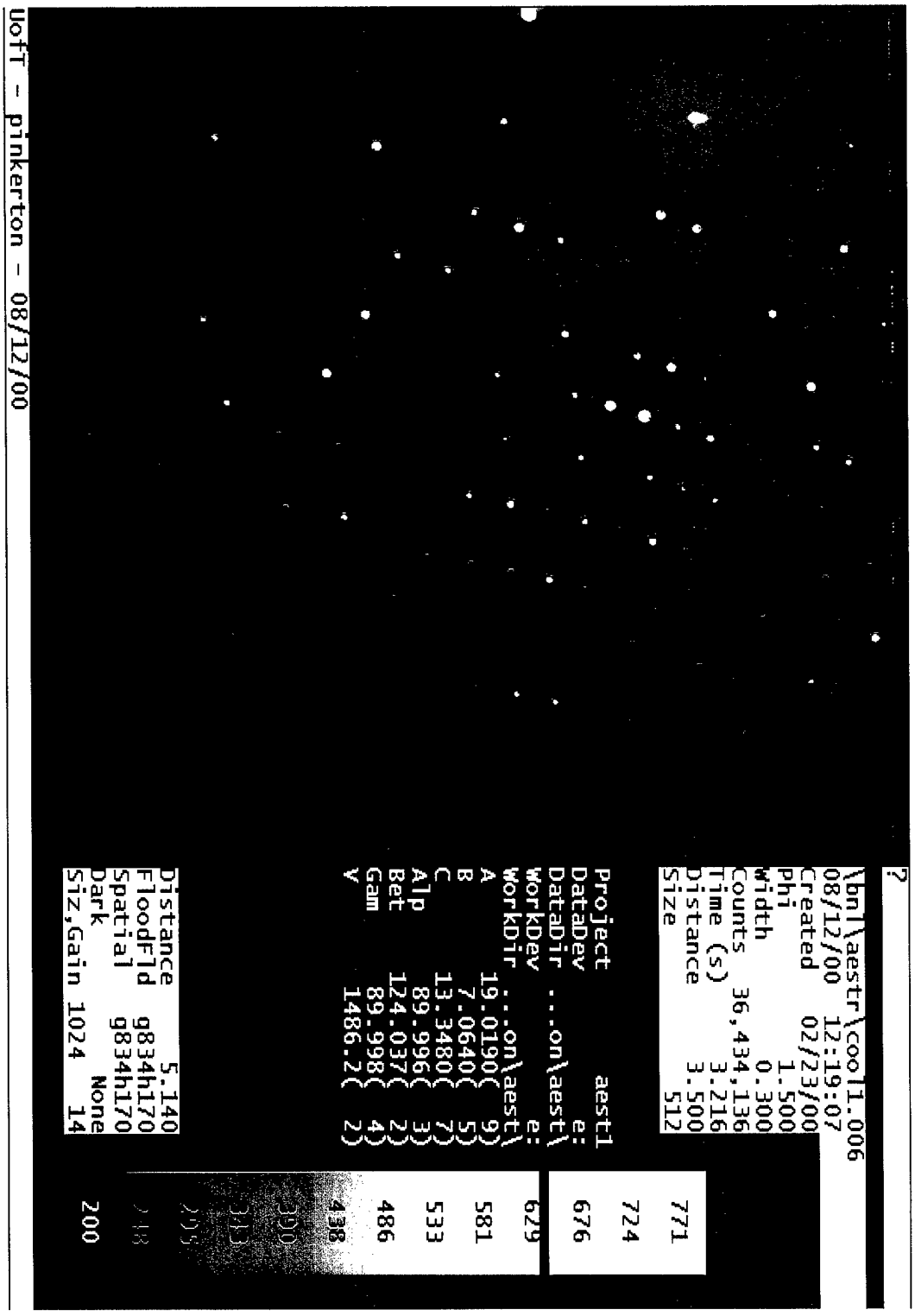
724
676
629
581
533
486
200
UofT - pinkerton - 08/12/00

Figure 1

Figure 2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A 19.0190(9)
B 7.0640(5)
C 13.3480(7)
Alp 89.996(3)
Bet 124.037(2)
Gam 89.998(4)
V 1486.2(2)
771
724
676
629
581
533
486
438
390
343
295
200
Distance 5.140
FloodFld g834h170
Spatial g834h170
Dark None
Siz,Gain 1024 14
UofT - pinkerton - 08/12/00

Appendix B

17α-estradiol•1/2 H_2O

Figure: Ortep drawing with 50 % probability ellipsoids of 17α-estradiol•1/2 H_2O

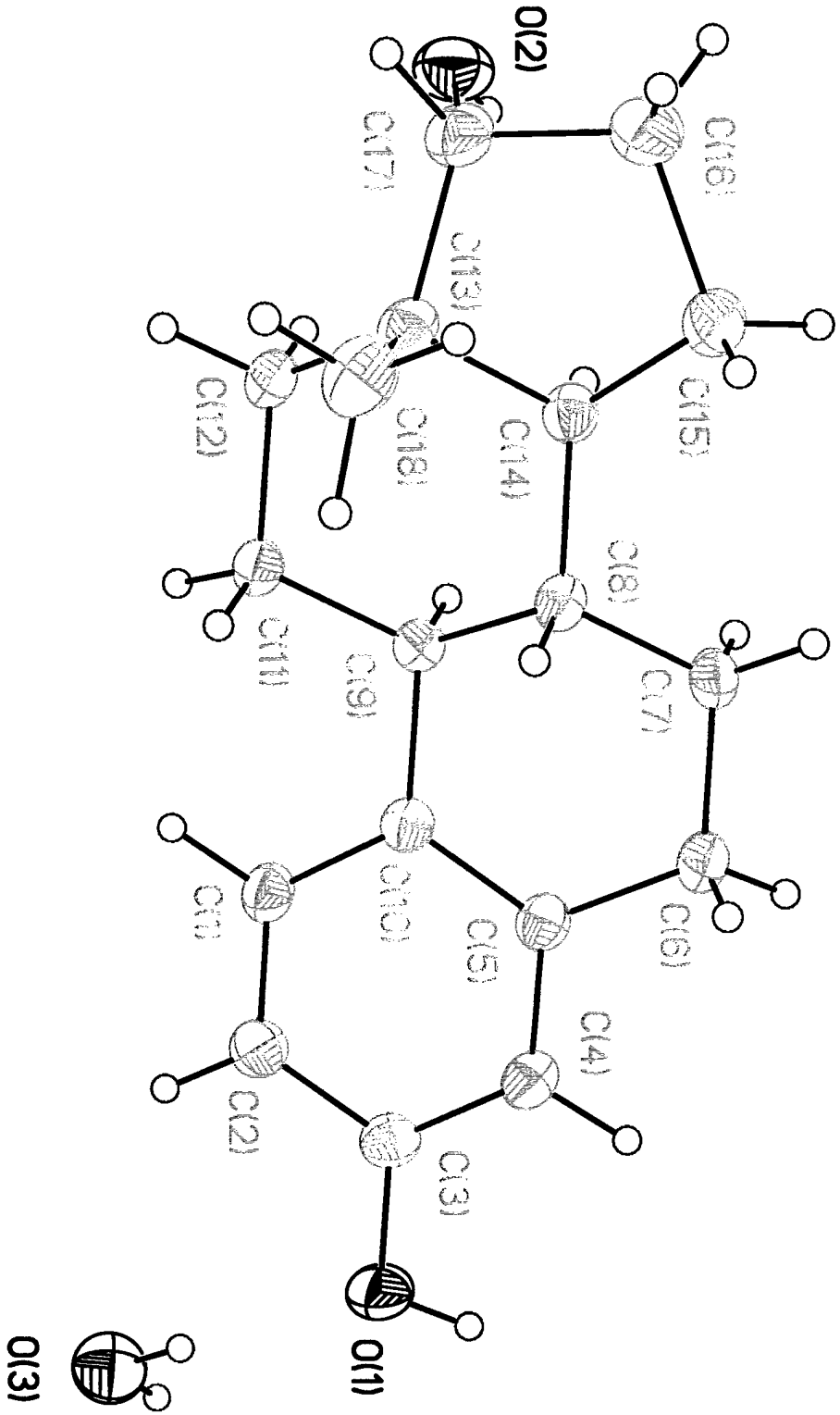

O(2)
C(17)
C(16)
C(13)
C(12)
C(18)
C(14)
C(15)
C(8)
C(11)
C(9)
C(7)
C(10)
C(12)
C(5)
C(6)
C(4)
C(2)
C(3)
O(1)
O(3)

Table 1. Crystal data and structure refinement for sad.

Identification code	sad
Empirical formula	C18 H25 O2.50
Formula weight	281.38
Temperature	293(2) K
Wavelength	0.56086 A
Crystal system, space group	monoclinic, C2
Unit cell dimensions	a = 19.2289(9) A alpha = 90 deg. b = 7.1425(3) A beta = 124.285(1) deg. c = 13.4258(6) A gamma = 90 deg.
Volume	1523.54(12) A^3
Z, Calculated density	4, 1.227 Mg/m^3
Absorption coefficient	0.051 mm^-1
F(000)	612
Theta range for data collection	1.45 to 20.50 deg.
Limiting indices	-24<=h<=17, -8<=k<=8, -12<=l<=16
Reflections collected / unique	4761 / 2818 [R(int) = 0.0328]
Completeness to theta = 20.50	96.4 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2818 / 1 / 286
Goodness-of-fit on F^2	0.945
Final R indices [I>2sigma(I)]	R1 = 0.0503, wR2 = 0.1132
R indices (all data)	R1 = 0.0650, wR2 = 0.1205
Absolute structure parameter	1(3)
Largest diff. peak and hole	0.177 and -0.232 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for sad.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1)	-3816(1)	4946(3)	-4043(2)	57(1)
O(2)	917(2)	3628(4)	5070(2)	63(1)
O(3)	-5000	2004(5)	-5000	69(1)
C(1)	-2395(2)	2919(3)	-1055(2)	44(1)
C(2)	-3051(2)	3089(4)	-2259(2)	48(1)
C(3)	-3152(2)	4762(4)	-2851(2)	42(1)
C(4)	-2595(2)	6196(4)	-2248(2)	43(1)
C(5)	-1924(2)	6028(3)	-1041(2)	39(1)
C(6)	-1304(2)	7612(4)	-462(2)	49(1)
C(7)	-674(2)	7439(3)	901(2)	41(1)
C(8)	-371(2)	5436(3)	1275(2)	35(1)
C(9)	-1122(2)	4168(3)	920(2)	34(1)
C(10)	-1827(1)	4357(3)	-423(2)	35(1)
C(11)	-854(2)	2134(3)	1325(2)	41(1)
C(12)	-153(2)	1982(3)	2674(2)	43(1)
C(13)	597(2)	3213(3)	3014(2)	40(1)
C(14)	282(2)	5241(3)	2624(2)	37(1)
C(15)	1090(2)	6410(5)	3251(3)	54(1)
C(16)	1706(2)	5329(5)	4440(3)	63(1)
C(17)	1267(2)	3481(4)	4365(2)	49(1)
C(18)	1050(2)	2459(5)	2450(3)	56(1)

Table 3. Bond lengths [A] and angles [deg] for sad.

O(1)-C(3)	1.381(3)
O(2)-C(17)	1.441(4)
C(1)-C(2)	1.387(4)
C(1)-C(10)	1.387(3)
C(2)-C(3)	1.387(4)
C(3)-C(4)	1.369(4)
C(4)-C(5)	1.397(3)
C(5)-C(10)	1.405(3)
C(5)-C(6)	1.503(4)
C(6)-C(7)	1.527(4)
C(7)-C(8)	1.519(3)
C(8)-C(14)	1.521(3)
C(8)-C(9)	1.535(3)
C(9)-C(10)	1.534(3)
C(9)-C(11)	1.535(3)
C(11)-C(12)	1.536(3)
C(12)-C(13)	1.522(3)
C(13)-C(17)	1.534(3)
C(13)-C(18)	1.539(4)
C(13)-C(14)	1.543(3)
C(14)-C(15)	1.532(4)
C(15)-C(16)	1.555(4)
C(16)-C(17)	1.539(4)
C(2)-C(1)-C(10)	122.3(2)
C(3)-C(2)-C(1)	119.0(3)
C(4)-C(3)-O(1)	121.2(2)
C(4)-C(3)-C(2)	119.7(2)
O(1)-C(3)-C(2)	119.1(2)
C(3)-C(4)-C(5)	121.7(2)
C(4)-C(5)-C(10)	119.1(2)
C(4)-C(5)-C(6)	118.7(2)
C(10)-C(5)-C(6)	122.1(2)
C(5)-C(6)-C(7)	114.9(2)
C(8)-C(7)-C(6)	111.7(2)
C(7)-C(8)-C(14)	112.7(2)
C(7)-C(8)-C(9)	109.50(19)
C(14)-C(8)-C(9)	108.46(17)
C(10)-C(9)-C(11)	113.41(18)
C(10)-C(9)-C(8)	111.52(17)
C(11)-C(9)-C(8)	112.29(19)
C(1)-C(10)-C(5)	118.11(19)
C(1)-C(10)-C(9)	121.6(2)
C(5)-C(10)-C(9)	120.3(2)
C(9)-C(11)-C(12)	112.40(19)
C(13)-C(12)-C(11)	111.53(19)
C(12)-C(13)-C(17)	116.72(19)
C(12)-C(13)-C(18)	110.7(2)
C(17)-C(13)-C(18)	107.1(2)
C(12)-C(13)-C(14)	108.42(19)
C(17)-C(13)-C(14)	101.1(2)
C(18)-C(13)-C(14)	112.6(2)
C(8)-C(14)-C(15)	120.4(2)
C(8)-C(14)-C(13)	113.2(2)
C(15)-C(14)-C(13)	104.0(2)
C(14)-C(15)-C(16)	104.1(2)
C(17)-C(16)-C(15)	106.6(2)
O(2)-C(17)-C(13)	113.2(2)
O(2)-C(17)-C(16)	109.7(3)
C(13)-C(17)-C(16)	104.4(2)

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for sad.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
O(1)	50(1)	62(1)	39(1)	7(1)	12(1)	-3(1)
O(2)	63(1)	77(2)	43(1)	3(1)	25(1)	-5(1)
O(3)	56(2)	75(2)	67(2)	0	29(2)	0
C(1)	44(1)	37(1)	47(1)	4(1)	23(1)	-5(1)
C(2)	41(2)	49(2)	44(1)	0(1)	19(1)	-8(1)
C(3)	36(1)	48(2)	38(1)	3(1)	18(1)	3(1)
C(4)	43(2)	41(1)	44(1)	8(1)	24(1)	4(1)
C(5)	39(1)	34(1)	41(1)	3(1)	21(1)	6(1)
C(6)	53(2)	32(1)	47(2)	6(1)	19(1)	-2(1)
C(7)	44(1)	28(1)	44(1)	-2(1)	22(1)	-2(1)
C(8)	36(1)	31(1)	39(1)	3(1)	21(1)	2(1)
C(9)	35(1)	32(1)	34(1)	1(1)	18(1)	1(1)
C(10)	31(1)	35(1)	38(1)	2(1)	19(1)	2(1)
C(11)	40(1)	33(1)	41(1)	3(1)	18(1)	-2(1)
C(12)	44(1)	32(1)	43(1)	7(1)	19(1)	1(1)
C(13)	36(1)	38(1)	43(1)	7(1)	20(1)	6(1)
C(14)	35(1)	35(1)	41(1)	1(1)	21(1)	2(1)
C(15)	42(2)	49(2)	54(2)	8(1)	16(1)	-6(1)
C(16)	43(2)	66(2)	56(2)	7(2)	13(1)	-9(2)
C(17)	38(1)	49(2)	48(1)	9(1)	18(1)	5(1)
C(18)	53(2)	52(2)	69(2)	9(1)	38(2)	17(2)

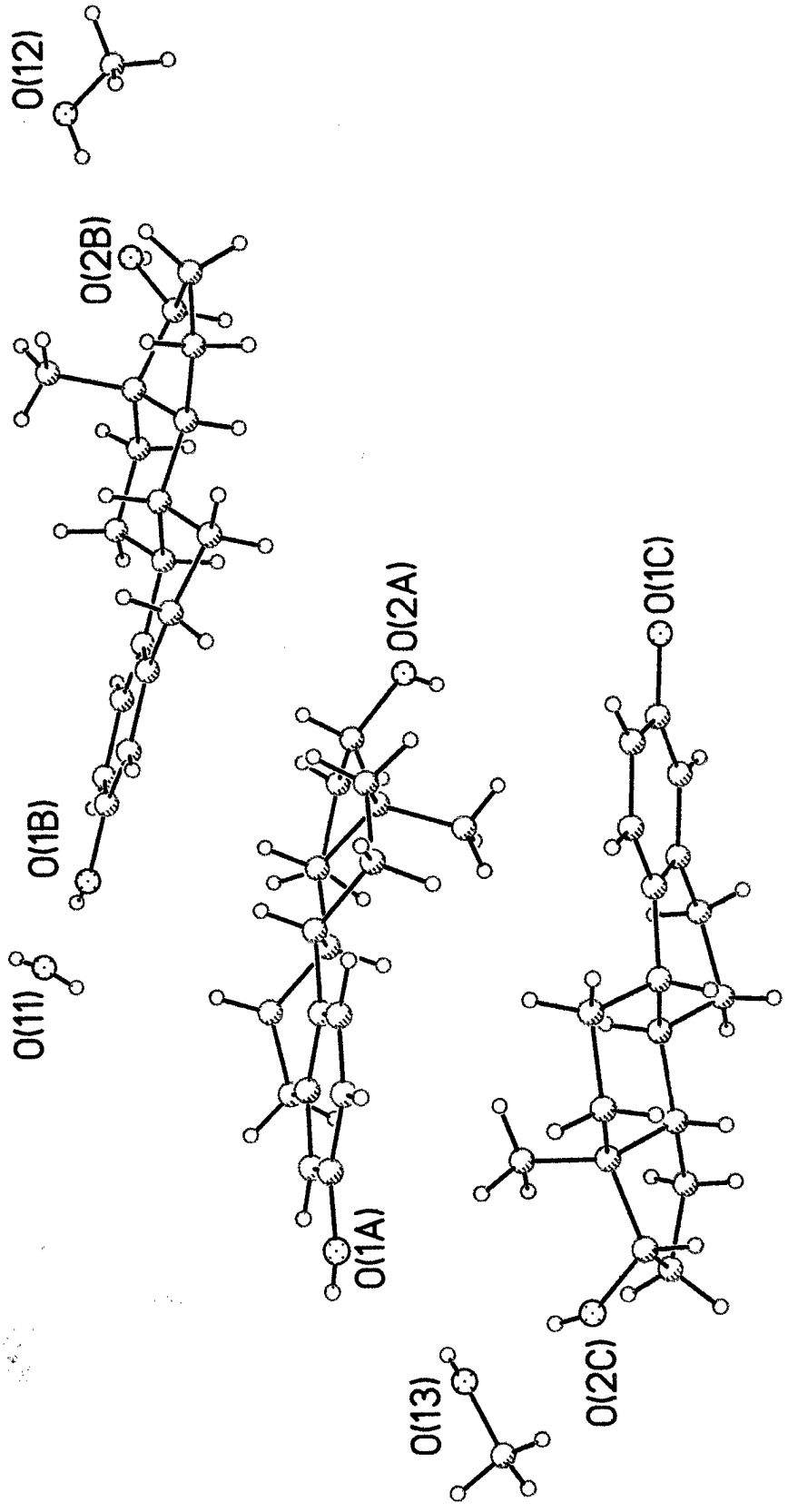
Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for sad.

	x	y	z	U(eq)
HO1	-3930(40)	6110(80)	-4250(50)	140(20)
HO2	610(40)	4190(110)	4900(50)	160(30)
HO3	-5420(50)	2750(130)	-5270(90)	260(40)
H(1)	-2347(15)	1700(40)	-640(20)	37(6)
H(2)	-3400(20)	2070(50)	-2660(30)	62(9)
H(4)	-2663(18)	7420(40)	-2620(20)	48(7)
H(6A)	-1590(20)	8810(50)	-620(30)	64(9)
H(6B)	-990(20)	7630(50)	-860(30)	77(10)
H(7A)	-198(16)	8290(40)	1192(19)	30(6)
H(7B)	-912(19)	7920(40)	1300(20)	55(8)
H(8)	-160(16)	4970(40)	780(20)	35(6)
H(9)	-1376(18)	4650(40)	1360(20)	48(7)
H(11A)	-1370(20)	1360(40)	1200(20)	56(8)
H(11B)	-677(17)	1620(40)	810(20)	41(7)
H(12A)	32(17)	650(40)	2900(20)	43(7)
H(12B)	-368(18)	2450(40)	3170(20)	46(7)
H(14)	12(18)	5600(40)	2970(20)	40(7)
H(15A)	960(20)	7720(50)	3410(30)	67(9)
H(15B)	1350(30)	6440(60)	2810(30)	88(12)
H(16A)	2240(30)	5120(60)	4530(30)	91(13)
H(16B)	1850(30)	6050(50)	5210(40)	90(12)
H(17)	1720(18)	2440(40)	4720(20)	48(8)
H(18A)	661(19)	2360(40)	1520(30)	52(8)
H(18B)	1230(20)	1350(60)	2720(30)	71(10)
H(18C)	1580(20)	3230(50)	2670(30)	74(10)

Appendix C

17β-estradiol•2/3 MeOH•1/3 H_2O

Figure: Ortep drawing of the molecules in the asymmetric unit of 17β-estradiol•2/3 MeOH•1/3 H_2O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O(2B)
O(1B)
O(11)
O(2A)
O(1C)
O(1A)
O(13)
O(2C)

Table 1. Crystal data and structure refinement for sad.

Identification code	sad
Empirical formula	C18 H20 O5
Formula weight	316.34
Temperature	100(2) K
Wavelength	0.71073 A
Crystal system, space group	monoclinic, P2(1)
Unit cell dimensions	a = 11.7129(4) A alpha = 90 deg. b = 19.6206(7) A beta = 117.975(1) deg. c = 12.1268(4) A gamma = 90 deg.
Volume	2461.27(15) A^3
Z, Calculated density	6, 1.281 Mg/m^3
Absorption coefficient	0.093 mm^-1
F(000)	1008
Theta range for data collection	1.90 to 39.45 deg.
Limiting indices	-19<=h<=20, -34<=k<=31, -21<=l<=21
Reflections collected / unique	46721 / 23160 [R(int) = 0.0495]
Completeness to theta = 39.45	91.8 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	23160 / 1 / 843
Goodness-of-fit on F^2	0.968
Final R indices [I>2sigma(I)]	R1 = 0.0611, wR2 = 0.1337
R indices (all data)	R1 = 0.0965, wR2 = 0.1471
Absolute structure parameter	-0.4(5)
Largest diff. peak and hole	0.447 and -0.249 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for sad.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1C)	9179(1)	6078(1)	2577(1)	24(1)
C(10C)	5660(1)	6515(1)	-579(1)	17(1)
C(55C)	6279(1)	7016(1)	345(1)	16(1)
C(4C)	7456(1)	6870(1)	1396(1)	17(1)
C(14C)	2649(1)	7481(1)	-2958(1)	17(1)
O(2C)	-413(1)	6892(1)	-5559(1)	25(1)
C(8C)	3736(1)	7311(1)	-1661(1)	15(1)
C(9C)	4446(1)	6682(1)	-1787(1)	17(1)
C(3C)	8022(1)	6230(1)	1558(1)	19(1)
C(13C)	1665(1)	6895(1)	-3534(1)	16(1)
C(1C)	6255(2)	5875(1)	-390(1)	21(1)
C(7C)	4689(2)	7900(1)	-1069(1)	20(1)
C(6C)	5691(2)	7714(1)	252(1)	20(1)
C(2C)	7419(2)	5727(1)	664(1)	22(1)
C(17C)	762(1)	7239(1)	-4783(1)	20(1)
C(12C)	2359(2)	6258(1)	-3629(2)	25(1)
C(16C)	590(2)	7969(1)	-4426(2)	26(1)
C(15C)	1813(2)	8118(1)	-3171(2)	25(1)
C(11C)	3510(2)	6076(1)	-2357(2)	28(1)
C(18C)	921(2)	6741(1)	-2808(1)	24(1)
O(1B)	1186(1)	4126(1)	3026(1)	25(1)
C(8B)	7061(1)	3350(1)	6935(1)	16(1)
C(14B)	8441(1)	3366(1)	7992(1)	18(1)
C(5B)	4605(1)	3685(1)	4863(1)	18(1)
C(6B)	5577(2)	3280(1)	4641(1)	22(1)
C(9B)	6301(1)	3944(1)	7109(1)	18(1)
C(3B)	2399(2)	4096(1)	4021(1)	20(1)
O(2B)	10424(1)	3080(1)	11364(1)	26(1)
C(11B)	6363(2)	3915(1)	8409(1)	21(1)
C(12B)	7760(2)	3877(1)	9480(1)	22(1)
C(4B)	3345(2)	3741(1)	3880(1)	19(1)
C(17B)	9975(2)	3311(1)	10100(1)	21(1)
C(10B)	4931(1)	3989(1)	6030(1)	17(1)
C(1B)	3958(2)	4351(1)	6138(1)	21(1)
C(15B)	9450(2)	2857(1)	8019(1)	24(1)
C(13B)	8499(1)	3287(1)	9282(1)	17(1)
C(7B)	6967(2)	3398(1)	5635(1)	22(1)
C(2B)	2711(2)	4413(1)	5158(1)	21(1)
C(18B)	7988(2)	2598(1)	9460(1)	22(1)
C(16B)	10507(2)	2854(1)	9412(2)	27(1)
C(8A)	2224(1)	5522(1)	1055(1)	17(1)
O(1A)	-1320(1)	4776(1)	-4769(1)	24(1)
C(9A)	2413(1)	4883(1)	408(1)	18(1)
C(5A)	232(1)	5221(1)	-1408(1)	17(1)
C(10A)	1408(1)	4866(1)	-971(1)	17(1)
C(11A)	3817(1)	4822(1)	631(1)	22(1)
O(2A)	6678(1)	5603(1)	4679(1)	26(1)

C(13A)	4610(1)	5487(1)	2653(1)	18(1)
C(7A)	823(1)	5548(1)	822(1)	21(1)
C(14A)	3207(1)	5491(1)	2436(1)	17(1)
C(1A)	1615(2)	4485(1)	-1842(1)	21(1)
C(3A)	-447(1)	4812(1)	-3517(1)	19(1)
C(12A)	4814(2)	4853(1)	2028(1)	23(1)
C(6A)	-86(1)	5661(1)	-565(1)	20(1)
C(4A)	-687(1)	5189(1)	-2675(1)	18(1)
C(2A)	707(2)	4454(1)	-3099(1)	22(1)
C(15A)	3189(2)	6036(1)	3337(1)	24(1)
C(16A)	4558(2)	5991(1)	4471(1)	25(1)
C(17A)	5317(1)	5479(1)	4095(1)	22(1)
C(18A)	4972(2)	6131(1)	2173(2)	22(1)
O(13)	-2460(1)	6940(1)	-5104(1)	25(1)
O(12)	11871(1)	2033(1)	12719(1)	27(1)
O(11)	-554(1)	4751(1)	3372(1)	30(1)
C(101)	-3190(2)	7492(1)	-5882(2)	27(1)
C(100)	12838(2)	1886(1)	12359(2)	31(1)

Table 3. Bond lengths [A] and angles [deg] for sad.

O(1C)-C(3C)	1.3722(18)
C(10C)-C(1C)	1.401(2)
C(10C)-C(55C)	1.4104(19)
C(10C)-C(9C)	1.5231(19)
C(55C)-C(4C)	1.3998(19)
C(55C)-C(6C)	1.512(2)
C(4C)-C(3C)	1.390(2)
C(14C)-C(8C)	1.5254(19)
C(14C)-C(15C)	1.533(2)
C(14C)-C(13C)	1.543(2)
O(2C)-C(17C)	1.4248(18)
C(8C)-C(7C)	1.531(2)
C(8C)-C(9C)	1.536(2)
C(9C)-C(11C)	1.544(2)
C(3C)-C(2C)	1.390(2)
C(13C)-C(12C)	1.525(2)
C(13C)-C(18C)	1.532(2)
C(13C)-C(17C)	1.538(2)
C(1C)-C(2C)	1.393(2)
C(7C)-C(6C)	1.521(2)
C(17C)-C(16C)	1.536(2)
C(12C)-C(11C)	1.540(2)
C(16C)-C(15C)	1.553(2)
O(1B)-C(3B)	1.3676(18)
C(8B)-C(14B)	1.521(2)
C(8B)-C(7B)	1.5305(19)
C(8B)-C(9B)	1.541(2)
C(14B)-C(15B)	1.535(2)
C(14B)-C(13B)	1.5411(19)
C(5B)-C(4B)	1.400(2)
C(5B)-C(10B)	1.4137(19)
C(5B)-C(6B)	1.513(2)
C(6B)-C(7B)	1.522(2)
C(9B)-C(10B)	1.524(2)
C(9B)-C(11B)	1.5441(19)
C(3B)-C(4B)	1.385(2)
C(3B)-C(2B)	1.396(2)
O(2B)-C(17B)	1.4408(19)
C(11B)-C(12B)	1.541(2)
C(12B)-C(13B)	1.530(2)
C(17B)-C(13B)	1.539(2)
C(17B)-C(16B)	1.541(2)
C(10B)-C(1B)	1.401(2)
C(1B)-C(2B)	1.391(2)
C(15B)-C(16B)	1.557(2)
C(13B)-C(18B)	1.535(2)
C(8A)-C(14A)	1.5246(18)
C(8A)-C(7A)	1.529(2)
C(8A)-C(9A)	1.549(2)
O(1A)-C(3A)	1.3781(17)
C(9A)-C(10A)	1.5291(19)
C(9A)-C(11A)	1.540(2)
C(5A)-C(4A)	1.4045(19)

C(5A)-C(10A)	1.407(2)
C(5A)-C(6A)	1.513(2)
C(10A)-C(1A)	1.403(2)
C(11A)-C(12A)	1.543(2)
O(2A)-C(17A)	1.4297(19)
C(13A)-C(18A)	1.533(2)
C(13A)-C(12A)	1.534(2)
C(13A)-C(14A)	1.537(2)
C(13A)-C(17A)	1.544(2)
C(7A)-C(6A)	1.527(2)
C(14A)-C(15A)	1.537(2)
C(1A)-C(2A)	1.392(2)
C(3A)-C(2A)	1.390(2)
C(3A)-C(4A)	1.393(2)
C(15A)-C(16A)	1.550(2)
C(16A)-C(17A)	1.545(2)
O(13)-C(101)	1.428(2)
O(12)-C(100)	1.421(2)

C(1C)-C(10C)-C(55C)	117.63(13)
C(1C)-C(10C)-C(9C)	121.30(12)
C(55C)-C(10C)-C(9C)	120.88(13)
C(4C)-C(55C)-C(10C)	120.03(13)
C(4C)-C(55C)-C(6C)	118.22(12)
C(10C)-C(55C)-C(6C)	121.74(12)
C(3C)-C(4C)-C(55C)	120.95(13)
C(8C)-C(14C)-C(15C)	120.57(12)
C(8C)-C(14C)-C(13C)	112.92(11)
C(15C)-C(14C)-C(13C)	104.36(12)
C(14C)-C(8C)-C(7C)	113.04(11)
C(14C)-C(8C)-C(9C)	107.53(11)
C(7C)-C(8C)-C(9C)	110.04(12)
C(10C)-C(9C)-C(8C)	112.52(11)
C(10C)-C(9C)-C(11C)	114.25(12)
C(8C)-C(9C)-C(11C)	111.04(12)
O(1C)-C(3C)-C(4C)	121.91(13)
O(1C)-C(3C)-C(2C)	118.23(14)
C(4C)-C(3C)-C(2C)	119.86(13)
C(12C)-C(13C)-C(18C)	110.39(14)
C(12C)-C(13C)-C(17C)	115.50(12)
C(18C)-C(13C)-C(17C)	109.82(12)
C(12C)-C(13C)-C(14C)	109.44(12)
C(18C)-C(13C)-C(14C)	113.13(12)
C(17C)-C(13C)-C(14C)	98.13(11)
C(2C)-C(1C)-C(10C)	122.39(14)
C(6C)-C(7C)-C(8C)	110.17(12)
C(55C)-C(6C)-C(7C)	113.31(12)
C(3C)-C(2C)-C(1C)	119.13(14)
O(2C)-C(17C)-C(16C)	114.70(13)
O(2C)-C(17C)-C(13C)	116.48(13)
C(16C)-C(17C)-C(13C)	104.63(12)
C(13C)-C(12C)-C(11C)	111.17(12)
C(17C)-C(16C)-C(15C)	105.56(13)
C(14C)-C(15C)-C(16C)	103.57(13)
C(12C)-C(11C)-C(9C)	112.00(14)
C(14B)-C(8B)-C(7B)	113.64(12)
C(14B)-C(8B)-C(9B)	108.84(11)

C(7B)-C(8B)-C(9B)	109.13(12)
C(8B)-C(14B)-C(15B)	120.50(12)
C(8B)-C(14B)-C(13B)	112.11(11)
C(15B)-C(14B)-C(13B)	104.27(11)
C(4B)-C(5B)-C(10B)	120.02(13)
C(4B)-C(5B)-C(6B)	118.10(12)
C(10B)-C(5B)-C(6B)	121.86(13)
C(5B)-C(6B)-C(7B)	113.19(12)
C(10B)-C(9B)-C(8B)	111.65(11)
C(10B)-C(9B)-C(11B)	113.89(12)
C(8B)-C(9B)-C(11B)	110.99(12)
O(1B)-C(3B)-C(4B)	118.23(13)
O(1B)-C(3B)-C(2B)	122.27(14)
C(4B)-C(3B)-C(2B)	119.50(14)
C(12B)-C(11B)-C(9B)	112.67(13)
C(13B)-C(12B)-C(11B)	111.04(12)
C(3B)-C(4B)-C(5B)	121.31(13)
O(2B)-C(17B)-C(13B)	114.55(13)
O(2B)-C(17B)-C(16B)	110.79(13)
C(13B)-C(17B)-C(16B)	104.55(12)
C(1B)-C(10B)-C(5B)	117.29(13)
C(1B)-C(10B)-C(9B)	121.60(12)
C(5B)-C(10B)-C(9B)	121.07(12)
C(2B)-C(1B)-C(10B)	122.66(13)
C(14B)-C(15B)-C(16B)	103.77(12)
C(12B)-C(13B)-C(18B)	111.02(13)
C(12B)-C(13B)-C(17B)	115.05(12)
C(18B)-C(13B)-C(17B)	109.24(12)
C(12B)-C(13B)-C(14B)	108.95(12)
C(18B)-C(13B)-C(14B)	113.37(12)
C(17B)-C(13B)-C(14B)	98.76(11)
C(6B)-C(7B)-C(8B)	109.84(12)
C(1B)-C(2B)-C(3B)	119.19(14)
C(17B)-C(16B)-C(15B)	105.50(13)
C(14A)-C(8A)-C(7A)	113.37(11)
C(14A)-C(8A)-C(9A)	108.01(11)
C(7A)-C(8A)-C(9A)	109.19(12)
C(10A)-C(9A)-C(11A)	113.63(12)
C(10A)-C(9A)-C(8A)	110.66(11)
C(11A)-C(9A)-C(8A)	111.67(12)
C(4A)-C(5A)-C(10A)	120.20(13)
C(4A)-C(5A)-C(6A)	117.35(13)
C(10A)-C(5A)-C(6A)	122.42(12)
C(1A)-C(10A)-C(5A)	117.65(13)
C(1A)-C(10A)-C(9A)	121.27(13)
C(5A)-C(10A)-C(9A)	121.07(12)
C(9A)-C(11A)-C(12A)	112.69(12)
C(18A)-C(13A)-C(12A)	110.25(12)
C(18A)-C(13A)-C(14A)	113.28(12)
C(12A)-C(13A)-C(14A)	108.72(12)
C(18A)-C(13A)-C(17A)	109.97(12)
C(12A)-C(13A)-C(17A)	115.24(12)
C(14A)-C(13A)-C(17A)	99.03(11)
C(6A)-C(7A)-C(8A)	109.97(12)
C(8A)-C(14A)-C(15A)	119.79(12)
C(8A)-C(14A)-C(13A)	112.64(11)
C(15A)-C(14A)-C(13A)	104.56(12)

C(2A)-C(1A)-C(10A)	122.31(14)
O(1A)-C(3A)-C(2A)	117.96(13)
O(1A)-C(3A)-C(4A)	122.23(14)
C(2A)-C(3A)-C(4A)	119.81(13)
C(13A)-C(12A)-C(11A)	111.20(12)
C(5A)-C(6A)-C(7A)	113.33(12)
C(3A)-C(4A)-C(5A)	120.69(14)
C(3A)-C(2A)-C(1A)	119.33(14)
C(14A)-C(15A)-C(16A)	103.75(13)
C(17A)-C(16A)-C(15A)	105.92(12)
O(2A)-C(17A)-C(13A)	116.12(13)
O(2A)-C(17A)-C(16A)	113.96(13)
C(13A)-C(17A)-C(16A)	104.47(12)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for sad.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
O(1C)	19(1)	26(1)	18(1)	-1(1)	2(1)	6(1)
C(10C)	16(1)	18(1)	15(1)	-2(1)	5(1)	2(1)
C(55C)	14(1)	18(1)	16(1)	-1(1)	7(1)	1(1)
C(4C)	14(1)	20(1)	16(1)	-1(1)	5(1)	0(1)
C(14C)	16(1)	17(1)	16(1)	1(1)	6(1)	-2(1)
O(2C)	16(1)	38(1)	17(1)	-5(1)	4(1)	-4(1)
C(8C)	14(1)	14(1)	15(1)	0(1)	5(1)	0(1)
C(9C)	16(1)	20(1)	14(1)	-2(1)	5(1)	2(1)
C(3C)	18(1)	22(1)	16(1)	1(1)	7(1)	3(1)
C(13C)	15(1)	18(1)	14(1)	-1(1)	5(1)	-2(1)
C(1C)	21(1)	19(1)	19(1)	-4(1)	6(1)	3(1)
C(7C)	19(1)	14(1)	21(1)	1(1)	4(1)	0(1)
C(6C)	17(1)	17(1)	19(1)	-4(1)	3(1)	1(1)
C(2C)	23(1)	20(1)	20(1)	-1(1)	7(1)	6(1)
C(17C)	16(1)	27(1)	15(1)	1(1)	5(1)	-1(1)
C(12C)	21(1)	25(1)	21(1)	-8(1)	4(1)	2(1)
C(16C)	18(1)	25(1)	25(1)	3(1)	2(1)	2(1)
C(15C)	20(1)	18(1)	26(1)	0(1)	1(1)	1(1)
C(11C)	25(1)	18(1)	27(1)	-6(1)	0(1)	3(1)
C(18C)	21(1)	33(1)	18(1)	1(1)	9(1)	-7(1)
O(1B)	20(1)	30(1)	19(1)	-3(1)	5(1)	7(1)
C(8B)	17(1)	17(1)	15(1)	-1(1)	8(1)	0(1)
C(14B)	18(1)	19(1)	17(1)	0(1)	9(1)	-1(1)
C(5B)	20(1)	19(1)	16(1)	-1(1)	9(1)	2(1)
C(6B)	21(1)	28(1)	16(1)	-2(1)	9(1)	5(1)
C(9B)	20(1)	16(1)	17(1)	-1(1)	9(1)	-1(1)
C(3B)	20(1)	19(1)	18(1)	0(1)	8(1)	3(1)
O(2B)	27(1)	27(1)	15(1)	-2(1)	4(1)	2(1)
C(11B)	23(1)	25(1)	16(1)	-2(1)	9(1)	5(1)
C(12B)	24(1)	22(1)	18(1)	-4(1)	9(1)	2(1)
C(4B)	21(1)	20(1)	17(1)	-1(1)	9(1)	3(1)
C(17B)	18(1)	24(1)	17(1)	0(1)	5(1)	-1(1)
C(10B)	20(1)	16(1)	17(1)	0(1)	9(1)	1(1)
C(1B)	23(1)	20(1)	18(1)	-3(1)	9(1)	3(1)
C(15B)	21(1)	34(1)	18(1)	-1(1)	9(1)	6(1)
C(13B)	17(1)	18(1)	15(1)	-1(1)	7(1)	-1(1)
C(7B)	21(1)	32(1)	16(1)	0(1)	11(1)	2(1)
C(2B)	21(1)	21(1)	21(1)	-2(1)	9(1)	5(1)
C(18B)	24(1)	22(1)	20(1)	3(1)	9(1)	-2(1)
C(16B)	18(1)	39(1)	21(1)	-3(1)	6(1)	5(1)
C(8A)	14(1)	19(1)	15(1)	0(1)	6(1)	0(1)
O(1A)	22(1)	28(1)	15(1)	-1(1)	4(1)	0(1)
C(9A)	16(1)	17(1)	16(1)	1(1)	4(1)	1(1)
C(5A)	17(1)	16(1)	16(1)	1(1)	7(1)	-1(1)
C(10A)	17(1)	16(1)	17(1)	-1(1)	6(1)	-2(1)
C(11A)	16(1)	26(1)	19(1)	-3(1)	5(1)	3(1)
O(2A)	17(1)	27(1)	24(1)	0(1)	1(1)	-2(1)
C(13A)	15(1)	20(1)	16(1)	2(1)	5(1)	-1(1)

C(7A)	16(1)	30(1)	16(1)	-1(1)	6(1)	0(1)
C(14A)	16(1)	21(1)	14(1)	1(1)	5(1)	-2(1)
C(1A)	19(1)	21(1)	19(1)	-2(1)	6(1)	2(1)
C(3A)	20(1)	18(1)	16(1)	-1(1)	7(1)	-3(1)
C(12A)	18(1)	25(1)	20(1)	0(1)	4(1)	2(1)
C(6A)	15(1)	24(1)	18(1)	-1(1)	5(1)	3(1)
C(4A)	16(1)	19(1)	16(1)	1(1)	5(1)	0(1)
C(2A)	22(1)	22(1)	20(1)	-5(1)	8(1)	-1(1)
C(15A)	21(1)	31(1)	18(1)	-5(1)	7(1)	-1(1)
C(16A)	22(1)	33(1)	16(1)	-3(1)	6(1)	-3(1)
C(17A)	17(1)	25(1)	17(1)	2(1)	2(1)	-3(1)
C(18A)	19(1)	24(1)	22(1)	2(1)	8(1)	-4(1)
O(13)	22(1)	28(1)	22(1)	-2(1)	8(1)	-2(1)
O(12)	24(1)	35(1)	25(1)	5(1)	13(1)	7(1)
O(11)	37(1)	28(1)	32(1)	8(1)	21(1)	12(1)
C(101)	25(1)	26(1)	28(1)	-6(1)	10(1)	0(1)
C(100)	23(1)	37(1)	34(1)	-1(1)	16(1)	3(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for sad.

	x	y	z	U(eq)
H(1CA)	9290(30)	6316(14)	3040(20)	35
H(4CA)	7880(20)	7233(11)	1975(19)	21
H(14A)	3010(20)	7534(11)	-3506(19)	20
H(8CA)	3390(20)	7190(11)	-1092(19)	18
H(9CA)	4700(20)	6818(11)	-2350(19)	21
H(1CB)	5830(20)	5522(12)	-1020(20)	25
H(7CA)	5080(20)	7969(11)	-1600(20)	24
H(7CB)	4260(20)	8304(12)	-1069(19)	24
H(6CA)	6370(20)	8063(11)	580(20)	24
H(6CB)	5280(20)	7727(11)	792(19)	24
H(2CB)	7730(20)	5311(12)	790(20)	27
H(17A)	1240(20)	7249(11)	-5250(20)	24
H(12A)	2690(20)	6344(12)	-4170(20)	30
H(12B)	1730(20)	5868(12)	-3970(20)	30
H(16A)	-130(20)	7975(12)	-4330(20)	31
H(16B)	470(20)	8305(12)	-5090(20)	31
H(15A)	2230(20)	8501(13)	-3200(20)	30
H(15B)	1590(20)	8199(13)	-2570(20)	30
H(11A)	3970(20)	5717(13)	-2430(20)	33
H(11B)	3190(20)	5907(13)	-1720(20)	33
H(18A)	200(30)	6407(13)	-3290(20)	36
H(18B)	480(30)	7176(13)	-2740(20)	36
H(18C)	1470(20)	6523(13)	-2030(20)	36
H(1BA)	750(30)	4319(14)	3190(20)	37
H(8BA)	6700(20)	2921(11)	6956(19)	19
H(14B)	8790(20)	3821(11)	7983(19)	21
H(6BA)	5460(20)	3382(11)	3830(20)	26
H(6BB)	5410(20)	2803(12)	4620(20)	26
H(9BA)	6740(20)	4369(11)	7095(19)	21
H(11C)	6000(20)	4306(11)	8590(20)	25
H(11D)	5880(20)	3514(12)	8440(20)	25
H(12C)	8230(20)	4302(12)	9580(20)	26
H(12D)	7740(20)	3802(12)	10290(20)	26
H(4BA)	3140(20)	3529(11)	3080(20)	23
H(17B)	10300(20)	3778(12)	10110(20)	25
H(1BB)	4140(20)	4553(12)	6940(20)	25
H(15C)	9860(20)	3004(12)	7450(20)	29
H(15D)	9070(20)	2387(13)	7750(20)	29
H(7BA)	7270(20)	3879(12)	5580(20)	27
H(7BB)	7540(20)	3090(12)	5510(20)	27
H(2BB)	2130(20)	4666(12)	5280(20)	25
H(18D)	8190(20)	2570(13)	10400(20)	34
H(18E)	8360(20)	2218(13)	9220(20)	34
H(18F)	7120(30)	2565(13)	8980(20)	34
H(16C)	10670(20)	2373(13)	9770(20)	33
H(16D)	11310(20)	3025(12)	9490(20)	33
H(8AA)	2400(20)	5926(11)	679(19)	20
H(1AA)	-1930(30)	5041(13)	-4920(20)	35
H(9AA)	2260(20)	4520(11)	810(20)	21

H(11E)	3980(20)	5228(12)	180(20)	26
H(11F)	3950(20)	4394(12)	280(20)	26
H(7AA)	610(20)	5134(12)	1080(20)	25
H(7AB)	740(20)	5905(12)	1350(20)	25
H(14C)	3070(20)	5054(11)	2742(19)	21
H(1AB)	2410(20)	4216(11)	-1600(20)	25
H(12E)	4750(20)	4467(12)	2480(20)	27
H(12F)	5740(20)	4850(12)	2100(20)	27
H(6AA)	-980(20)	5598(12)	-807(19)	24
H(6AB)	-110(20)	6123(12)	-800(20)	24
H(4AA)	-1470(20)	5421(11)	-2995(19)	21
H(2AB)	860(20)	4217(11)	-3720(20)	26
H(15E)	2560(20)	5946(12)	3610(20)	29
H(15F)	3080(20)	6500(12)	3000(20)	29
H(16E)	5000(20)	6424(12)	4670(20)	30
H(16F)	4550(20)	5876(12)	5160(20)	30
H(17C)	5240(20)	5016(11)	4360(20)	26
H(18G)	5840(20)	6118(13)	2380(20)	33
H(18H)	4870(20)	6546(13)	2500(20)	33
H(18I)	4530(20)	6172(12)	1270(20)	33
H(10B)	-4120(20)	7503(13)	-5930(20)	33
H(10A)	13420(30)	2290(14)	12470(20)	37
H(110)	-610(30)	5115(17)	3220(30)	46(8)
H(2CA)	-880(20)	6908(12)	-5300(20)	28(6)
H(111)	-710(30)	4734(14)	3910(30)	37(7)
H(130)	-2330(20)	7035(13)	-4420(20)	35(6)
H(2AA)	6800(20)	5960(12)	4655(19)	19(5)
H(122)	12490(20)	1755(13)	11560(20)	29(6)
H(121)	-2770(20)	7905(12)	-5580(20)	25(5)
H(120)	-3330(20)	7429(12)	-6680(20)	30(6)
H(2BA)	10590(20)	3362(13)	11790(20)	26(6)
H(123)	11410(30)	2322(14)	12290(20)	32(6)
H(124)	13350(30)	1548(14)	12810(20)	41(7)

Appendix D

17β-estradiol•1/2 MeOH

Figure: Ortep drawing of the molecules in the asymmetric unit of 17β-estradiol•1/2 MeOH

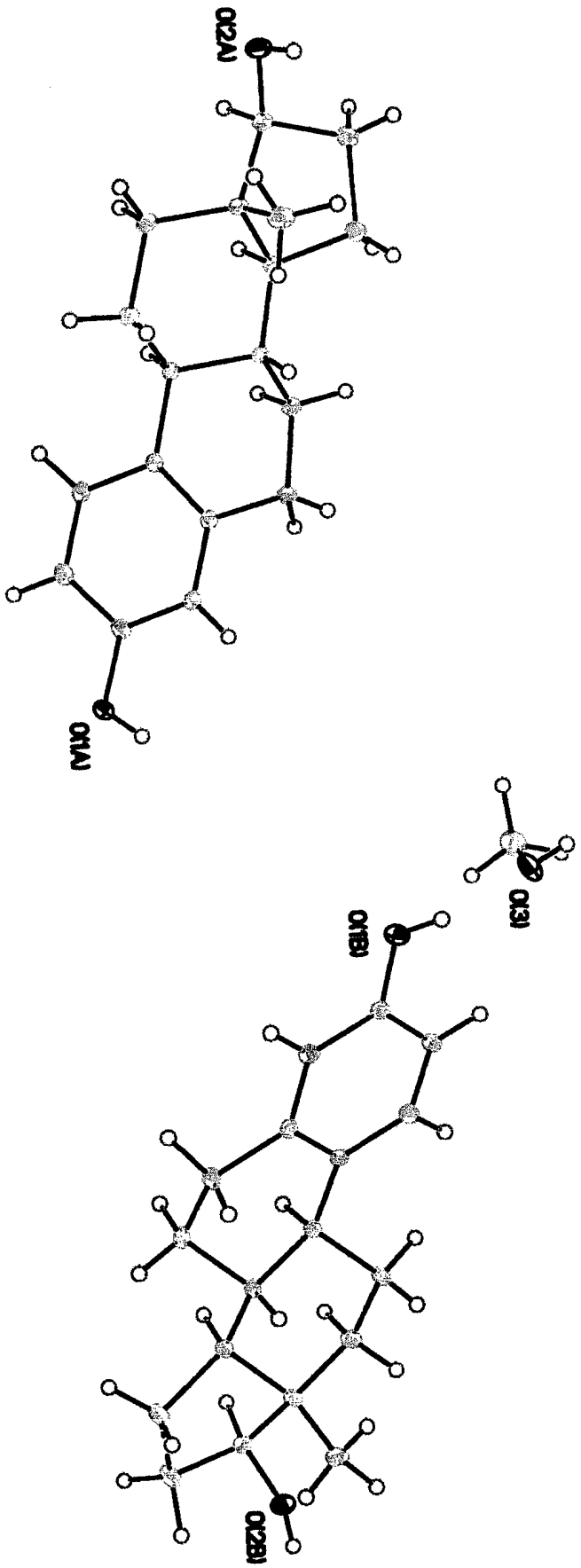
O24A
O1A0
O1B1
O31
O23B1

Table 1. Crystal data and structure refinement.

Empirical formula	C18.50 H25 O2.50
Formula weight	287.39
Temperature	100(1) K
Wavelength	0.71073 A
Crystal system, space group	triclinic, P1
Unit cell dimensions	a = 7.3073(15) A alpha = 89.45(3) deg. b = 9.2950(19) A beta = 87.86(3) deg. c = 12.418(3) A gamma = 70.78(3) deg.
Volume	795.9(3) A^3
Z, Calculated density	2, 1.199 Mg/m^3
Absorption coefficient	0.078 mm^-1
F(000)	312
Theta range for data collection	2.32 to 30.10 deg.
Limiting indices	-10<=h<=10, -12<=k<=13, -17<=l<=17
Reflections collected / unique	19615 / 8276 [R(int) = 0.0295]
Completeness to theta = 30.10	92.8 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8276 / 3 / 587
Goodness-of-fit on F^2	0.824
Final R indices [I>2sigma(I)]	R1 = 0.0392, wR2 = 0.1038
R indices (all data)	R1 = 0.0454, wR2 = 0.1076
Absolute structure parameter	-1.1(6)
Largest diff. peak and hole	0.303 and -0.230 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for ?.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1B)	6125(2)	7316(1)	7743(1)	21(1)
C(14B)	8596(2)	4628(2)	1655(1)	17(1)
C(4B)	7954(2)	6423(2)	6123(1)	18(1)
O(2B)	6350(2)	4684(1)	-967(1)	22(1)
C(8B)	8495(2)	5437(2)	2729(1)	16(1)
C(10B)	6429(2)	6115(2)	4473(1)	16(1)
C(5B)	8111(2)	6012(2)	5034(1)	16(1)
C(9B)	6578(2)	5482(2)	3329(1)	16(1)
C(1B)	4637(2)	6705(2)	5027(1)	19(1)
C(13B)	6887(2)	5422(2)	927(1)	16(1)
O(3)	2488(2)	8132(2)	8534(1)	31(1)
C(12B)	4982(2)	5500(2)	1528(1)	20(1)
C(11B)	4812(2)	6268(2)	2642(1)	20(1)
C(6B)	10100(2)	5519(2)	4471(1)	20(1)
C(7B)	10203(2)	4618(2)	3433(1)	20(1)
C(3B)	6158(2)	6967(2)	6663(1)	18(1)
C(17B)	7478(2)	4281(2)	-20(1)	18(1)
C(2B)	4471(2)	7153(2)	6105(1)	20(1)
C(16B)	9668(2)	4004(2)	-217(1)	25(1)
C(15B)	10408(2)	4319(2)	890(1)	24(1)
C(18B)	6820(2)	7020(2)	562(1)	22(1)
O(1A)	9750(2)	151(1)	9819(1)	25(1)
C(14A)	5493(2)	1042(2)	15858(1)	17(1)
O(2A)	6877(2)	1663(1)	18604(1)	24(1)
C(8A)	5910(2)	1213(2)	14661(1)	16(1)
C(9A)	7948(2)	96(2)	14351(1)	16(1)
C(5A)	6915(2)	652(2)	12403(1)	17(1)
C(10A)	8408(2)	154(2)	13141(1)	17(1)
C(7A)	4426(2)	884(2)	13946(1)	20(1)
C(13A)	6996(2)	1352(2)	16585(1)	17(1)
C(4A)	7354(2)	648(2)	11296(1)	18(1)
C(11A)	9512(2)	306(2)	15076(1)	22(1)
C(12A)	8999(2)	205(2)	16284(1)	21(1)
C(1A)	10327(2)	-349(2)	12720(1)	22(1)
C(6A)	4789(2)	1248(2)	12770(1)	20(1)
C(2A)	10770(2)	-355(2)	11622(1)	25(1)
C(3A)	9277(2)	151(2)	10903(1)	20(1)
C(16A)	3901(2)	1880(2)	17601(1)	27(1)
C(17A)	6127(2)	1117(2)	17697(1)	20(1)
C(15A)	3534(2)	2000(2)	16375(1)	27(1)
C(18A)	7046(3)	2986(2)	16502(1)	25(1)
C(19)	1700(3)	6911(2)	8587(2)	32(1)

Table 3. Bond lengths [A] and angles [deg] for ?.

O(1B)-C(3B)	1.3805(17)
C(14B)-C(8B)	1.5251(19)
C(14B)-C(13B)	1.545(2)
C(14B)-C(15B)	1.548(2)
C(4B)-C(3B)	1.390(2)
C(4B)-C(5B)	1.399(2)
O(2B)-C(17B)	1.4363(18)
C(8B)-C(7B)	1.531(2)
C(8B)-C(9B)	1.5500(18)
C(10B)-C(1B)	1.399(2)
C(10B)-C(5B)	1.4106(18)
C(10B)-C(9B)	1.5290(19)
C(5B)-C(6B)	1.5172(19)
C(9B)-C(11B)	1.541(2)
C(1B)-C(2B)	1.395(2)
C(13B)-C(12B)	1.535(2)
C(13B)-C(18B)	1.535(2)
C(13B)-C(17B)	1.5426(19)
O(3)-C(19)	1.431(2)
C(12B)-C(11B)	1.545(2)
C(6B)-C(7B)	1.530(2)
C(3B)-C(2B)	1.396(2)
C(17B)-C(16B)	1.545(2)
C(16B)-C(15B)	1.560(2)
O(1A)-C(3A)	1.3769(17)
C(14A)-C(8A)	1.5238(19)
C(14A)-C(15A)	1.535(2)
C(14A)-C(13A)	1.546(2)
O(2A)-C(17A)	1.4371(18)
C(8A)-C(7A)	1.534(2)
C(8A)-C(9A)	1.5462(19)
C(9A)-C(10A)	1.5320(19)
C(9A)-C(11A)	1.543(2)
C(5A)-C(4A)	1.400(2)
C(5A)-C(10A)	1.4062(19)
C(5A)-C(6A)	1.521(2)
C(10A)-C(1A)	1.4057(19)
C(7A)-C(6A)	1.529(2)
C(13A)-C(12A)	1.535(2)
C(13A)-C(18A)	1.534(2)
C(13A)-C(17A)	1.542(2)
C(4A)-C(3A)	1.397(2)
C(11A)-C(12A)	1.543(2)
C(1A)-C(2A)	1.390(2)
C(2A)-C(3A)	1.392(2)
C(16A)-C(17A)	1.554(2)
C(16A)-C(15A)	1.553(2)

C(8B)-C(14B)-C(13B)	113.55(11)
C(8B)-C(14B)-C(15B)	120.20(12)
C(13B)-C(14B)-C(15B)	103.82(11)
C(3B)-C(4B)-C(5B)	121.17(13)
C(14B)-C(8B)-C(7B)	112.26(11)
C(14B)-C(8B)-C(9B)	107.61(11)
C(7B)-C(8B)-C(9B)	109.12(12)
C(1B)-C(10B)-C(5B)	117.77(12)
C(1B)-C(10B)-C(9B)	121.22(12)
C(5B)-C(10B)-C(9B)	120.82(12)
C(4B)-C(5B)-C(10B)	119.85(12)
C(4B)-C(5B)-C(6B)	118.67(12)
C(10B)-C(5B)-C(6B)	121.43(12)
C(10B)-C(9B)-C(11B)	114.50(12)

C(10B)-C(9B)-C(8B)	112.06(11)
C(11B)-C(9B)-C(8B)	111.15(11)
C(2B)-C(1B)-C(10B)	122.48(13)
C(12B)-C(13B)-C(18B)	110.14(13)
C(12B)-C(13B)-C(17B)	114.86(12)
C(18B)-C(13B)-C(17B)	111.08(12)
C(12B)-C(13B)-C(14B)	108.86(11)
C(18B)-C(13B)-C(14B)	113.67(12)
C(17B)-C(13B)-C(14B)	97.79(11)
C(13B)-C(12B)-C(11B)	111.22(12)
C(9B)-C(11B)-C(12B)	111.98(12)
C(5B)-C(6B)-C(7B)	113.36(12)
C(8B)-C(7B)-C(6B)	110.34(12)
O(1B)-C(3B)-C(4B)	117.74(13)
O(1B)-C(3B)-C(2B)	122.54(13)
C(4B)-C(3B)-C(2B)	119.71(13)
O(2B)-C(17B)-C(13B)	116.75(12)
O(2B)-C(17B)-C(16B)	114.55(12)
C(13B)-C(17B)-C(16B)	104.27(12)
C(1B)-C(2B)-C(3B)	118.88(13)
C(17B)-C(16B)-C(15B)	105.29(12)
C(14B)-C(15B)-C(16B)	103.28(12)
C(8A)-C(14A)-C(15A)	119.73(12)
C(8A)-C(14A)-C(13A)	113.22(11)
C(15A)-C(14A)-C(13A)	103.74(12)
C(14A)-C(8A)-C(7A)	112.82(11)
C(14A)-C(8A)-C(9A)	108.86(11)
C(7A)-C(8A)-C(9A)	108.69(11)
C(10A)-C(9A)-C(11A)	114.24(11)
C(10A)-C(9A)-C(8A)	111.28(11)
C(11A)-C(9A)-C(8A)	111.70(11)
C(4A)-C(5A)-C(10A)	120.46(12)
C(4A)-C(5A)-C(6A)	117.62(12)
C(10A)-C(5A)-C(6A)	121.90(12)
C(1A)-C(10A)-C(5A)	117.43(13)
C(1A)-C(10A)-C(9A)	121.51(13)
C(5A)-C(10A)-C(9A)	121.00(12)
C(6A)-C(7A)-C(8A)	110.17(12)
C(12A)-C(13A)-C(18A)	110.34(13)
C(12A)-C(13A)-C(14A)	108.22(11)
C(18A)-C(13A)-C(14A)	113.51(12)
C(12A)-C(13A)-C(17A)	115.61(12)
C(18A)-C(13A)-C(17A)	109.57(12)
C(14A)-C(13A)-C(17A)	99.27(11)
C(3A)-C(4A)-C(5A)	120.75(13)
C(12A)-C(11A)-C(9A)	112.16(12)
C(13A)-C(12A)-C(11A)	111.01(12)
C(2A)-C(1A)-C(10A)	122.35(14)
C(5A)-C(6A)-C(7A)	113.62(12)
C(3A)-C(2A)-C(1A)	119.51(14)
O(1A)-C(3A)-C(2A)	118.52(13)
O(1A)-C(3A)-C(4A)	121.99(13)
C(2A)-C(3A)-C(4A)	119.48(13)
C(17A)-C(16A)-C(15A)	105.82(12)
O(2A)-C(17A)-C(13A)	115.56(12)
O(2A)-C(17A)-C(16A)	113.01(13)
C(13A)-C(17A)-C(16A)	104.76(12)
C(14A)-C(15A)-C(16A)	103.66(13)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for ?.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
O(1B)	24(1)	25(1)	15(1)	-1(1)	0(1)	-9(1)
C(14B)	14(1)	21(1)	16(1)	-1(1)	2(1)	-5(1)
C(4B)	18(1)	19(1)	17(1)	2(1)	-2(1)	-8(1)
O(2B)	29(1)	24(1)	15(1)	1(1)	-4(1)	-10(1)
C(8B)	11(1)	20(1)	17(1)	1(1)	0(1)	-5(1)
C(10B)	14(1)	18(1)	15(1)	3(1)	-1(1)	-6(1)
C(5B)	13(1)	17(1)	18(1)	3(1)	-1(1)	-5(1)
C(9B)	13(1)	21(1)	14(1)	0(1)	1(1)	-6(1)
C(1B)	14(1)	24(1)	17(1)	1(1)	0(1)	-6(1)
C(13B)	18(1)	20(1)	13(1)	-1(1)	-1(1)	-7(1)
O(3)	28(1)	30(1)	32(1)	-8(1)	13(1)	-7(1)
C(12B)	17(1)	29(1)	16(1)	0(1)	-2(1)	-9(1)
C(11B)	13(1)	30(1)	17(1)	-1(1)	0(1)	-6(1)
C(6B)	11(1)	29(1)	20(1)	0(1)	-3(1)	-4(1)
C(7B)	12(1)	24(1)	20(1)	0(1)	-1(1)	-1(1)
C(3B)	21(1)	17(1)	16(1)	2(1)	0(1)	-7(1)
C(17B)	21(1)	20(1)	14(1)	-1(1)	-1(1)	-6(1)
C(2B)	18(1)	22(1)	19(1)	1(1)	3(1)	-6(1)
C(16B)	23(1)	30(1)	20(1)	-6(1)	5(1)	-7(1)
C(15B)	18(1)	32(1)	21(1)	-4(1)	4(1)	-6(1)
C(18B)	28(1)	19(1)	18(1)	1(1)	-1(1)	-9(1)
O(1A)	21(1)	33(1)	16(1)	-2(1)	2(1)	-1(1)
C(14A)	15(1)	21(1)	16(1)	2(1)	-1(1)	-6(1)
O(2A)	33(1)	22(1)	16(1)	0(1)	-5(1)	-8(1)
C(8A)	13(1)	18(1)	15(1)	3(1)	-1(1)	-4(1)
C(9A)	13(1)	20(1)	15(1)	1(1)	-1(1)	-4(1)
C(5A)	15(1)	17(1)	18(1)	1(1)	-2(1)	-5(1)
C(10A)	14(1)	18(1)	17(1)	0(1)	1(1)	-4(1)
C(7A)	15(1)	29(1)	17(1)	4(1)	-2(1)	-9(1)
C(13A)	20(1)	17(1)	14(1)	1(1)	-2(1)	-7(1)
C(4A)	15(1)	21(1)	17(1)	0(1)	-3(1)	-4(1)
C(11A)	14(1)	35(1)	15(1)	-1(1)	-2(1)	-6(1)
C(12A)	18(1)	27(1)	17(1)	1(1)	-5(1)	-6(1)
C(1A)	14(1)	29(1)	19(1)	-1(1)	-2(1)	-1(1)
C(6A)	13(1)	32(1)	16(1)	2(1)	-1(1)	-6(1)
C(2A)	18(1)	31(1)	22(1)	-3(1)	2(1)	-3(1)
C(3A)	20(1)	21(1)	16(1)	-3(1)	2(1)	-4(1)
C(16A)	23(1)	39(1)	18(1)	-1(1)	2(1)	-7(1)
C(17A)	23(1)	21(1)	16(1)	1(1)	-1(1)	-8(1)
C(15A)	18(1)	42(1)	18(1)	1(1)	3(1)	-5(1)
C(18A)	37(1)	21(1)	21(1)	2(1)	-2(1)	-14(1)
C(19)	30(1)	38(1)	30(1)	1(1)	5(1)	-14(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for ?.

	x	y	z	U(eq)
H(12D)	3920(30)	6130(20)	1107(16)	19(4)
H(7A)	4610(30)	-240(20)	14043(17)	26(5)
H(1A)	11400(30)	-700(20)	13209(16)	19(4)
H(6A)	4330(30)	2300(30)	12656(17)	28(5)
H(9A)	7860(20)	-960(20)	14521(14)	15(4)
H(11A)	10710(40)	-510(30)	14950(20)	41(6)
H(14B)	8500(30)	3620(20)	1854(15)	17(4)
H(16A)	3240(30)	1180(20)	18008(17)	29(5)
H(6D)	11110(30)	4980(20)	5000(18)	30(5)
H(12C)	4950(30)	4390(30)	1627(18)	32(5)
H(7C)	10100(30)	3580(20)	3629(15)	18(4)
H(17B)	7270(30)	3300(20)	281(16)	20(4)
H(6C)	10400(20)	6490(20)	4272(14)	13(4)
H(15B)	2490(40)	1550(30)	16170(20)	49(7)
H(18A)	8120(30)	3100(20)	16980(16)	24(5)
H(15C)	10840(30)	5300(30)	839(19)	39(6)
H(9B)	6650(30)	4370(20)	3411(16)	20(4)
H(15A)	3230(30)	3030(30)	16118(18)	34(6)
H(8B)	8550(20)	6470(20)	2599(14)	10(4)
H(18E)	6600(30)	7770(20)	1191(15)	19(4)
H(2B)	3240(30)	7540(20)	6469(17)	25(5)
H(7D)	11460(30)	4530(30)	3086(18)	33(5)
H(6B)	4090(30)	820(20)	12276(17)	28(5)
H(1B)	3460(30)	6850(20)	4687(16)	21(4)
H(17A)	6460(30)	0(20)	17850(17)	23(5)
H(12A)	9960(30)	330(20)	16713(18)	30(5)
H(11C)	3630(30)	6230(20)	3035(14)	15(4)
H(14A)	5700(30)	-50(20)	16012(15)	15(4)
H(2A)	12090(30)	-690(30)	11353(19)	37(6)
H(7B)	3110(30)	1460(20)	14199(17)	25(5)
H(16D)	10370(30)	2950(30)	-504(19)	37(6)
H(4B)	9190(30)	6350(30)	6503(19)	33(5)
H(8A)	5890(30)	2230(20)	14512(17)	27(5)
H(18D)	7910(40)	7100(30)	180(20)	46(7)
H(16C)	9910(30)	4740(30)	-780(20)	39(6)
H(15D)	11390(30)	3450(30)	1181(18)	33(5)
H(11B)	9740(30)	1280(30)	14909(17)	30(5)
H(4A)	6350(30)	965(19)	10800(15)	13(4)
H(18B)	5930(30)	3680(30)	16736(18)	32(5)
H(11D)	4710(30)	7430(20)	2545(16)	24(5)
H(3AA)	1920(30)	8760(30)	8920(20)	36(6)
H(2BB)	6630(30)	5390(30)	-1290(20)	33(6)
H(18C)	7340(30)	3230(30)	15790(20)	40(6)
H(12B)	9020(30)	-870(20)	16438(16)	23(5)
H(1BB)	4960(30)	7680(20)	7924(18)	27(5)
H(19C)	1790(50)	6480(40)	9300(30)	70(9)
H(1AA)	8850(30)	660(20)	9476(17)	23(5)
H(16B)	3430(30)	2940(30)	17934(18)	32(5)
H(18F)	5770(30)	7440(30)	85(19)	36(6)
H(2AA)	6500(30)	2510(30)	18593(18)	25(5)
H(19B)	390(40)	7340(30)	8450(20)	52(7)
H(19A)	2380(40)	6190(30)	8090(20)	50(7)

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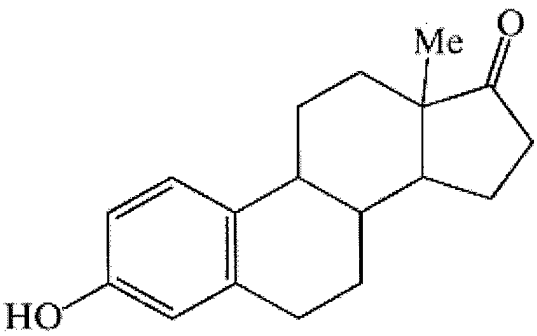


$\cdot 0.5CH_3OH$

Estradiol methanol hemisolvate

D. A. Parrish and A. A. Pinkerton

Synopsis: Initiation and progress of the majority of breast cancer cases are influenced by a family of hormones called estrogens. Estradiol is one of the three naturally occurring estrogens. This submission reports estradiol in a previously unknown crystal modification as the methanol hemisolvate.

Formula: $C_{18}H_{24}O_2 0.5CH_4O$

Appendix E

Estrone

Charge Density Study of Estrone

Damon Parrish, Nan Wu, Elizabeth Zhurova, and A. Alan Pinkerton

Department of Chemistry, University of Toledo

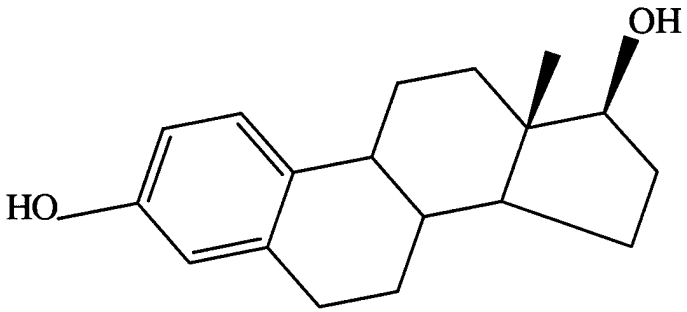
Introduction

The American Cancer Society predicts there will be 182,800 (~1500 of which will be men) new cases of breast cancer in the year 2000.[1] More than half of all breast cancers are known to be hormone dependent, and the family of hormones most responsible are the estrogens. Estrogens are a family of hormones which are primarily responsible for the development of primary and secondary sexual characteristics in females.

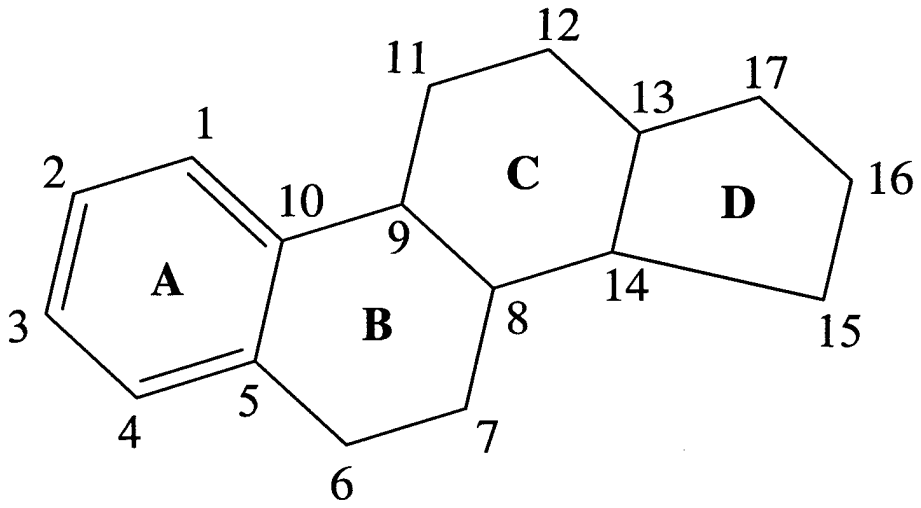
It has been known that estrogens play an essential role in the development of breast cancer. These derivatives and related compounds bind as ligands to the estrogen receptor and initiate a series of events resulting in the activation or repression of selective genes. The mechanism by which the ligands regulate the gene expression is currently unknown, however, it has been suggested that their characteristic electrostatic potentials are responsible. The three native derivatives and their naming scheme are shown in Fig 1.

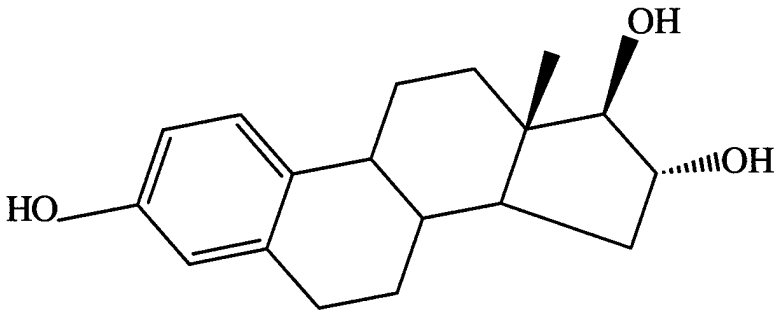
The goal of our investigation is to perform comparative electron density studies on a series of estrogen derivatives. This would allow us to directly compare the electrostatic potentials in an attempt to understand the relationship between this property and the biological activity of the specific compound.

Estrone is the first of the series to be completed and will be discussed in this poster.

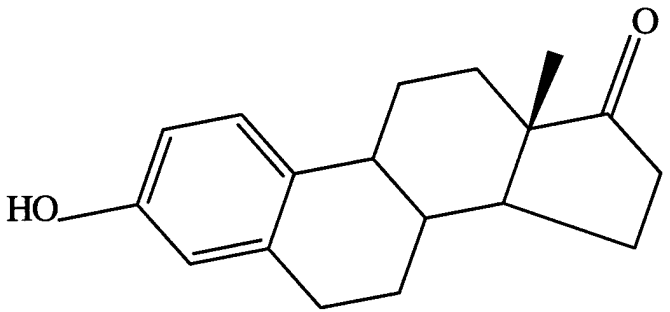


17β-estradiol





estriol



estrone

Figure 1

Experimental

The crystals were grown from an ethanol:ethyl acetate solution by slow evaporation. The data were collected at 92K on a Bruker 2k CCD diffractometer system with monochromatic Ag K_α radiation. To utilize the maximum dynamic range of our detector, 88 sec frames were used for the low angle data. This ensures that the most intense reflection will not be lost during the 8x retake. The complete data collection protocol can be seen in table 1. Due to the different frame times, low-angle data and high-angle data were integrated separately using SAINT 7[2]. The data was then merged and scaled in SORTAV[3], producing an HKL file containing all reflections to be used in XD. An absorption correction was performed using SADABS[4]. The structure was solved by direct methods using SHELXS[5a]. The coordinates and anisotropic thermal parameters of non-hydrogen atoms and the coordinates and isotropic thermal parameters of hydrogen atoms were refined by conventional least squares methods using SHELXL-97[5b]. This gave the starting point for the model that was subsequently used in XD.

Table 1. Data collection protocol

Run No.	2θ (deg.)	ω (deg.)	ϕ (deg.)	χ (deg.)	Scan Axis	Width (deg.)	Frames	Time/ frame (sec.)
1	-20	-20	0	54.74	Omega	-0.20	900	88
2	-20	-20	90	54.74	Omega	-0.20	900	88
3	-20	-20	180	54.74	Omega	-0.20	900	88
4	-20	-20	270	54.74	Omega	-0.20	900	88
5	-20	-20	0	54.74	Omega	-0.20	100	88
6	-65	-60	45	54.74	Omega	-0.20	900	180
7	-65	-60	135	54.74	Omega	-0.20	900	180
8	-65	-60	225	54.74	Omega	-0.20	900	180
9	-65	-60	315	54.74	Omega	-0.20	900	180

Table 2. Experimental

Compound name:	estrone	Data collection parameters:		
Chemical formula:	$C_{18}H_{22}O_2$	Temperature:		92.0(2)
Formula weight:	270.36	Radiation(Å):		AgK_α (0.56086)
Crystal density:	1.263	h_{min}/h_{max}		-20/20
			k_{min}/k_{max}	-26/25
Unit cell parameters:			l_{min}/l_{max}	-48/48
a (Å)	7.7618(1)	$\theta_{min}/\theta_{max}$		1.75/48.26
b (Å)	9.9536(1)	Total reflections:		27787
c (Å)	18.4055(1)	Observed reflections:		11466
V ($Å^3$)	1421.97(2)	R_{all}		0.0252
Z	4	$R_{\sin\theta/\lambda \leq 1.0\ Å^{-1}}$		0.0224

Multipole Refinement

XD is the program which was used for the multipole refinement.[6] As stated earlier, the HKL file from SORTAV and the coordinates and thermal parameters from SHELXL-97, were the starting point for the multipole refinement in XD. The coordinate system used for estrone can be seen in Figure 2. Intensity cutoffs for reflections of $\sin\theta/\lambda \leq 0.7$ Å^{-1} [$I > 2\sigma(I)$] and $\sin\theta/\lambda > 0.7$ Å^{-1} [$I > 6\sigma(I)$] were used throughout the refinement.

XD uses the Hansen-Coppens formalism[7] (equation 1), the atomic densities are described in terms of the spherical core and valence densities and an expansion of atom-centered spherical harmonic functions:

$$\rho_{atom}(r) = \rho_{core}(r) + P_v\kappa^3\rho_{valence}(\kappa r) + \sum_{l=1}^{lmax} \kappa'^3 R_l(\kappa' r) \sum_{m=0}^{l} P_{lm\pm} d_{lm\pm}(\theta,\phi)$$

Equation 1.

Below is a brief description of the steps involved in this refinement.

1. Refined coordinates and thermal parameters.
2. Input reasonable starting values for kappas.
3. With chemical constraints on, kappas and charges were alternately refined. See Figure S1 for details on chemical constraints.
4. Chemical constraints were removed (except for hydrogens), alternately refined kappas and charges. When finished fixed kappas and charges
5. Refined multipoles with mirror symmetry on sp^2 carbons.
6. Released sp^2 mirror symmetry, keeping hydrogens constrained.
7. Refined κ, κ', multipole, thermal, scale, charge, coordinates, in alternating fashion.
8. Eventually hydrogens released of most constraints, keeping hydrogens bound to same carbon equal.
9. Set multipole populations whose value was less than one standard deviation to zero.

The electrostatic potential was calculated using an isolated atom model in direct space.[8] The equation is shown below.

$$V(r) = \sum_A \frac{Z_A}{|R_A - r|} - \int \frac{\rho(r')dr'}{|r'-r|}$$

Equation 2.

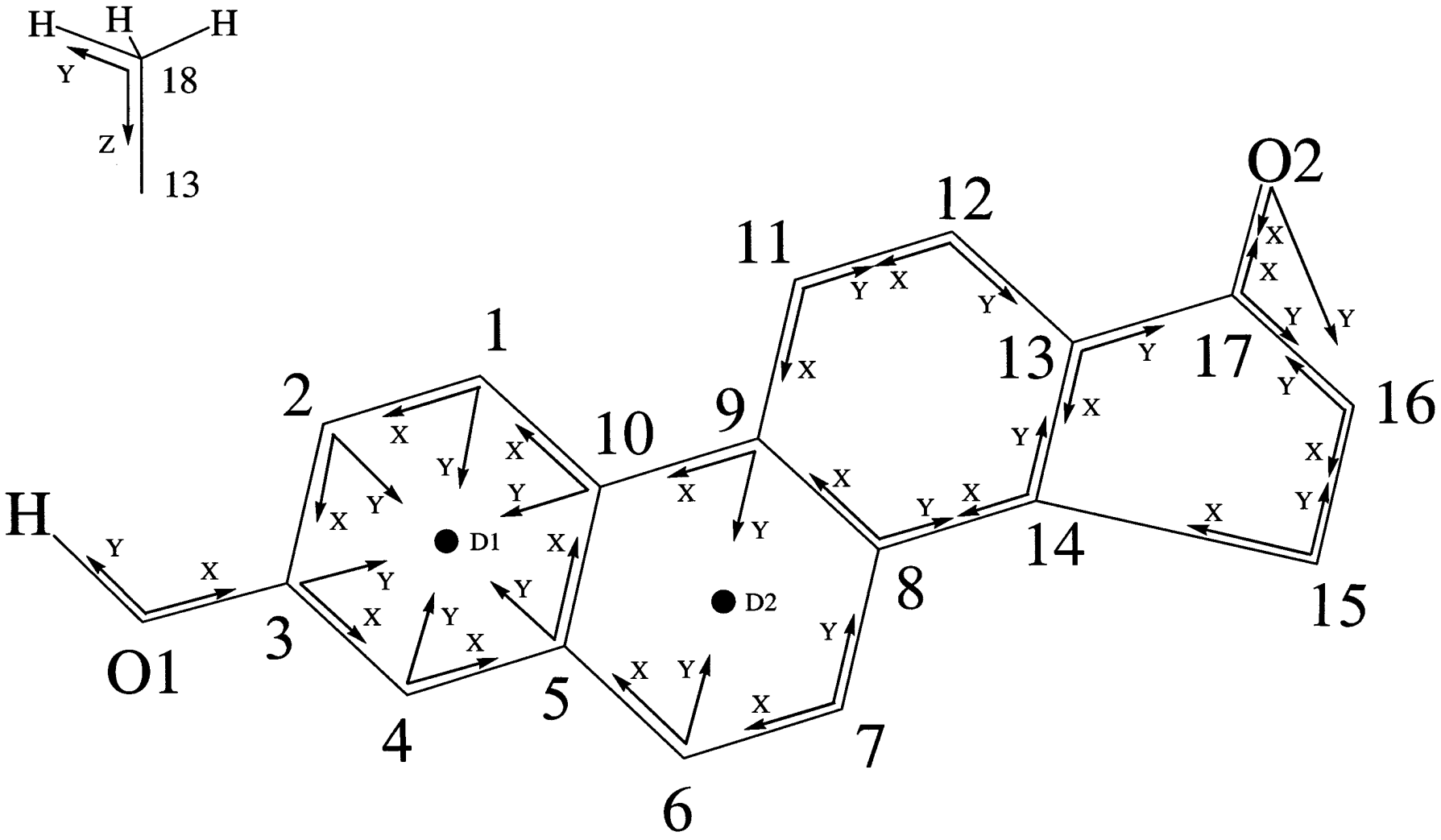
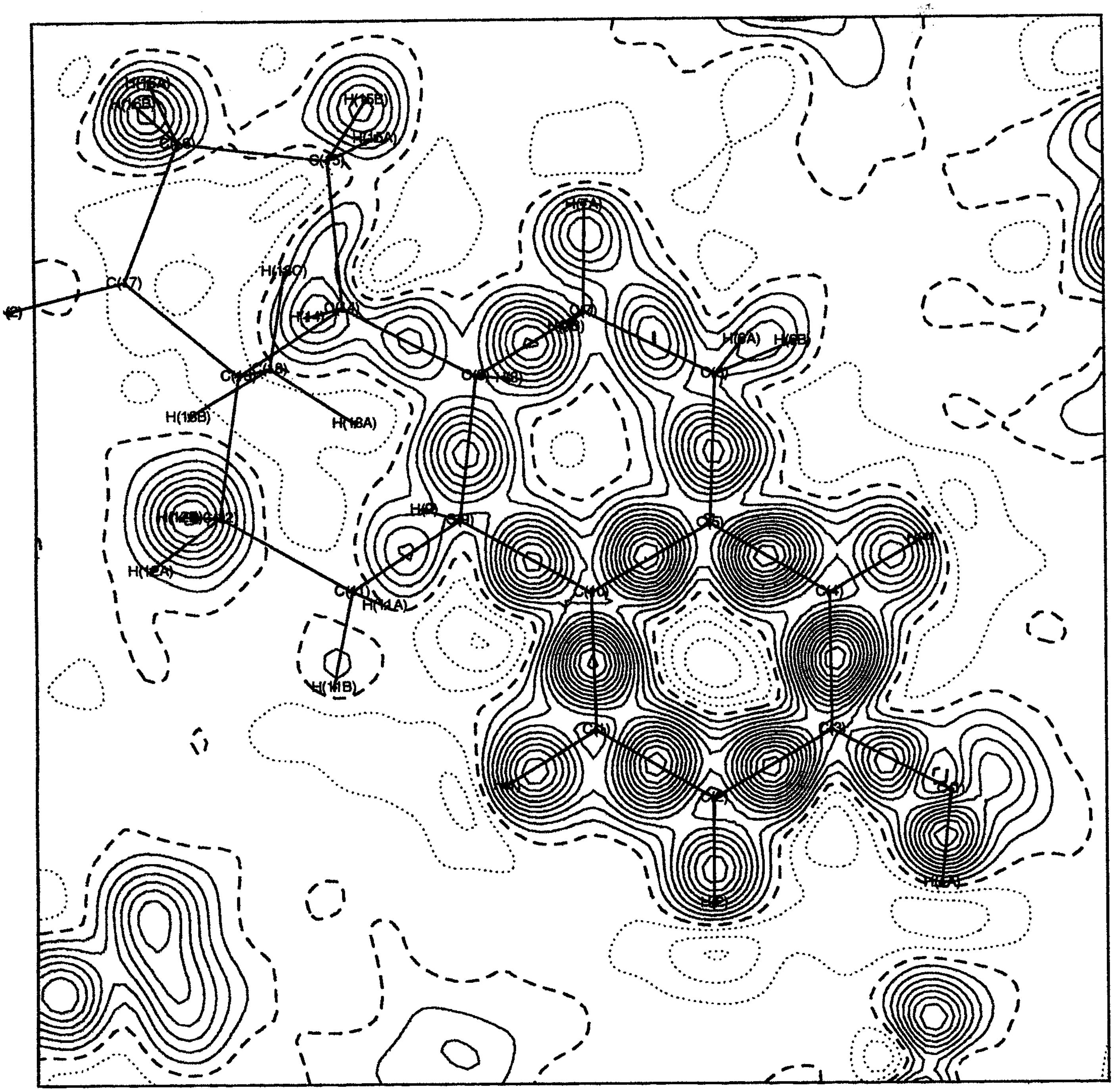


Figure 2. Local Coordinate System

Results

Atomic charges and multipole populations are reported in Tables 2 and 3. Deformation densities projected on the A and D rings are shown in Figures 3 and 4. Isosurfaces of the electrostatic potential are presented in Figure 5.

Figure 3



H(7A)
H(6A)
H(6B)
C(17)
H(18C)
H(18B)
H(18A)
H(12A)
C(11)
H(11A)
H(11B)
C(10)
C(4)
C(3)
C(2)
H(2)

Figure 4

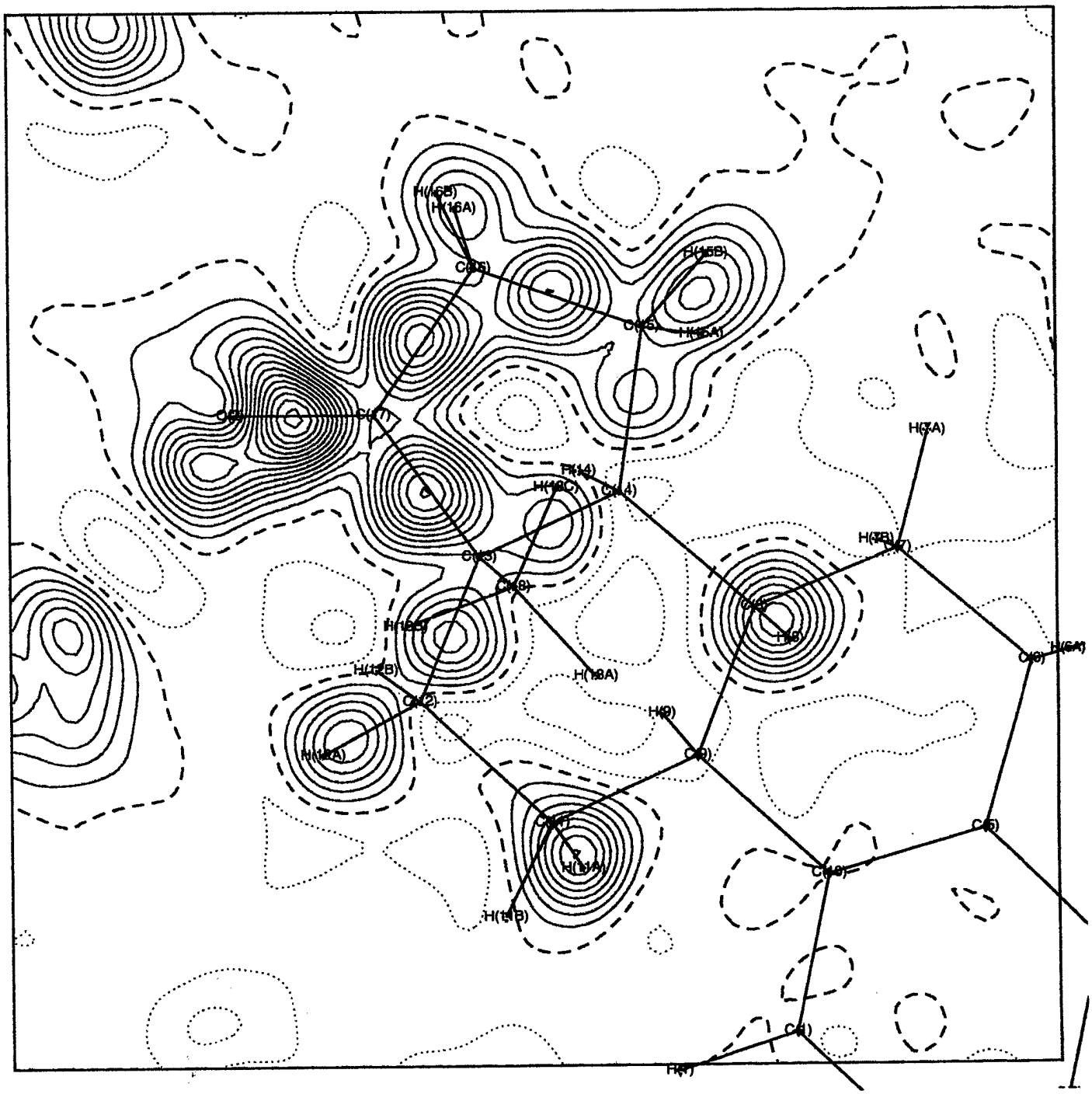

H(16B)
H(16A)
C(15)
H(15B)
O(5)
H(15A)
O(4)
C(17)
H(14)
H(13C)
C(14)
H(7A)
H(7B)
C(7)
C(13)
C(18)
C(12)
H(8)
H(6A)
O(6)
H(13B)
H(18A)
C(2)
H(9)
C(9)
H(12A)
C(11)
C(3)
C(10)
H(11A)
H(11B)
C(1)
H(1)

Figure 5

Table 2. Atomic Charges and κ' Parameters

Atom	O(1)	O(2)	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)
q, e	-0.524(8)	-0.413(8)	-0.47(1)	-0.48(1)	+0.32(1)	-0.46(1)	-0.20(1)	-0.33(1)	-0.41(1)	-0.16(1)	-0.15(1)
κ'	0.963(1)	0.977(1)	0.943(2)	0.943(2)	0.990(4)	0.943(2)	0.961(3)	0.969(1)	0.969(1)	0.969(1)	0.969(1)

Atom	C(10)	C(11)	C(12)	C(13)	C(14)	C(15)	C(16)	C(17)	C(18)	H(1A)	H(1)
q, e	-0.20(1)	-0.45(1)	-0.48(1)	+0.03(1)	-0.14(1)	-0.38(1)	-0.49(1)	+0.12(1)	-0.55(1)	+0.426(8)	+0.271(8)
κ'	0.961(3)	0.969(1)	0.969(1)	0.969(1)	0.969(1)	0.969(1)	0.969(1)	1.000(4)	0.969(1)	1.2	1.2

Atom	H(2)	H(4)	H(6A)	H(6B)	H(7A)	H(7B)	H(8)	H(9)	H(11A)	H(11B)
q, e	+0.298(8)	+0.336(8)	+0.342(6)	+0.342(6)	+0.284(6)	+0.284(6)	+0.271(8)	+0.200(8)	+0.244(6)	+0.244(6)
κ'	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2

Atom	H(12A)	H(12B)	H(14)	H(15A)	H(15B)	H(16A)	H(16B)	H(18A)	H(18B)	H(18C)
q, e	+0.165(6)	+0.165(6)	+0.223(8)	+0.259(6)	+0.259(6)	+0.243(6)	+0.243(6)	+0.238(5)	+0.238(5)	+0.238(5)
κ'	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2

Table 3. Multipole Population Parameters for Non-Hydrogen Atoms

Atom	κ'	D1+	D1-	D0	Q0	Q1+	Q1-	Q2+	Q2-	O0	O1+	O1-
O(1)	0.86(2)	-0.123(8)	0.036(8)				-0.042(9)	-0.070(9)	-0.020(9)			-0.08(1)
O(2)	0.79(2)	0.061(8)	-0.073(8)	-0.042(9)	-0.22(1)		-0.02(1)		0.07(1)	-0.01(1)		
C(1)	0.774(5)		0.03(2)	-0.07(1)	-0.40(2)							
C(2)	0.774(5)	0.02(1)			-0.39(2)		0.01(1)	0.06(1)	-0.01(1)		-0.06(2)	
C(3)	0.82(1)		0.03(2)		-0.18(2)	0.01(1)			0.03(2)	-0.05(2)	0.15(2)	0.12(2)
C(4)	0.774(5)	-0.15(2)		-0.03(1)	-0.40(2)		-0.09(1)		-0.17(2)	0.04(2)	0.14(3)	-0.12(2)
C(5)	0.836(7)		0.09(2)	-0.02(1)	-0.25(2)	-0.03(1)		-0.08(2)	-0.06(2)		0.02(2)	-0.05(2)
C(6)	0.800(3)	-0.04(1)			-0.06(1)		-0.05(1)	-0.06(1)		0.21(2)	-0.10(2)	-0.33(2)
C(7)	0.800(3)	-0.08(1)	-0.07(1)	-0.02(1)	0.02(1)	0.07(1)	-0.03(1)	-0.07(2)			-0.17(2)	-0.26(2)
C(8)	0.800(3)	0.05(2)		0.05(2)		-0.06(2)	-0.09(2)	-0.07(2)	0.03(2)	0.04(2)	-0.15(2)	-0.28(2)
C(9)	0.800(3)	-0.16(2)	-0.01(1)	-0.11(2)	-0.03(2)	0.05(2)	0.08(1)	-0.04(2)	-0.02(2)	-0.28(2)		-0.17(2)
C(10)	0.836(7)	-0.03(2)	0.03(2)	0.06(2)	-0.29(1)		0.05(1)			-0.02(2)		-0.04(2)
C(11)	0.800(3)	-0.05(2)	-0.05(2)	0.04(2)		0.04(2)			0.12(2)		-0.21(2)	-0.21(2)
C(12)	0.800(3)	-0.06(2)	-0.07(2)	-0.06(2)	-0.08(2)		-0.03(2)	-0.06(2)	0.07(2)	-0.05(2)	-0.20(2)	-0.25(2)
C(13)	0.800(3)	0.06(2)	0.12(2)	-0.04(2)	-0.02(2)	0.04(2)		-0.11(2)		0.08(3)	-0.20(2)	-0.29(2)
C(14)	0.800(3)	-0.10(2)	-0.04(2)	-0.03(2)		0.07(2)		0.05(2)	0.02(2)	-0.11(2)	-0.17(2)	-0.31(2)
C(15)	0.800(3)	-0.11(2)	-0.13(2)	0.06(2)	-0.06(2)	0.08(2)	0.03(2)		0.13(2)	0.05(2)	-0.18(2)	-0.19(2)
C(16)	0.800(3)		-0.04(2)	0.03(2)	-0.13(2)	0.03(2)	-0.04(2)	-0.05(1)	0.07(2)	-0.07(2)	-0.21(2)	-0.25(2)
C(17)	0.86(1)	0.07(1)			-0.20(1)	-0.02(1)		0.11(2)	-0.06(2)	-0.04(2)		0.05(2)
C(18)	0.800(3)	0.02(1)	-0.02(1)	-0.13(1)	0.04(2)	0.05(2)	0.07(2)	-0.02(2)	-0.04(1)	0.51(2)	0.10(2)	0.04(2)

Table 3 cont.

Atom	O2+	O2-	O3+	O3-	H0	H1+	H1-	H2+	H2-	H3+	H3-	H4+	H4-
O(1)	-0.03(1)		0.09(1)	-0.04(1)		0.05(2)				0.04(2)		0.04(1)	0.05(1)
O(2)	0.02(1)		0.06(1)		0.05(2)			0.01(1)	-0.05(2+	-0.03(2)			-0.05(1)
C(1)		0.07(2)	0.42(2)	0.07(2)	0.11(2)		0.02(2)	-0.05(2)		-0.10(3)	0.09(2)		
C(2)			0.45(2)		0.08(2)	-0.06(2)	0.05(2)	-0.06(2)	0.09(2)	-0.04(3)	0.13(2)		-0.04(2)
C(3)	0.06(2)	0.07(2)	0.51(2)				0.05(2)	0.13(2)	-0.02(2)	0.05(2)		-0.04(3)	
C(4)			0.40(2)		0.17(3)	0.06(2)		0.12(3)	0.14(3)		0.11(2)	-0.13(3)	-0.09(2)
C(5)			0.44(2)	-0.12(2)	0.03(2)		-0.04(2)	0.09(3)	0.10(2)	-0.06(2)			0.04(2)
C(6)	0.08(2)	0.12(2)	0.03(2)	0.30(2)	0.12(2)	-0.01(2)	-0.09(2)	-0.18(2)	-0.04(2)	0.06(2)			
C(7)			0.32(2)	-0.15(2)			-0.03(2)		0.22(3)	0.02(2)			
C(8)	0.06(2)		0.26(2)	-0.15(2)	0.05(3)	-0.10(3)		0.11(3)	0.18(3)	0.07(3)		0.17(3)	0.09(3)
C(9)	-0.06(2)	-0.13(2)		0.27(2)	0.18(3)	0.05(2)	0.08(2)	-0.05(3)	-0.08(2)	-0.06(2)	0.08(3)	-0.03(3)	0.07(3)
C(10)		-0.04(2)	0.42(2)	-0.03(2)	0.18(2)	-0.08(2)			-0.03(3)	0.06(3)		0.07(3)	-0.06(3)
C(11)	0.03(2)		0.29(2)	-0.08(2)		-0.12(2)	-0.10(2)	-0.08(3)	0.04(3)		0.04(3)	-0.05(2)	
C(12)	0.02(2)		0.34(2)	-0.08(2)	0.14(2)	-0.03(2)	-0.03(2)		0.10(3)	0.17(2)	-0.09(3)	0.07(2)	
C(13)			0.22(2)	-0.13(2)	0.14(3)	-0.09(3)	-0.04(3)		0.19(3)	-0.12(3)	0.03(3)	0.09(3)	
C(14)	0.06(2)	0.06(2)	0.27(2)	-0.19(2)	0.07(3)	-0.05(3)	0.05(3)	-0.10(3)	0.15(3)	0.19(3)	-0.11(3)	-0.06(2)	0.11(3)
C(15)	0.13(2)	0.05(2)	0.26(2)	-0.18(2)		-0.03(3)	-0.12(2)	0.05(2)		-0.08(3)	0.21(3)	-0.05(3)	
C(16)	0.03(2)	0.07(2)	0.29(2)	-0.07(2)	0.06(2)		0.11(2)	0.02(2)	0.25(3)	0.07(2)			0.04(2)
C(17)	0.03(2)	-0.02(2)	0.37(2)		-0.03(2)		0.02(2)	0.03(3)	0.04(3)	0.11(2)			
C(18)	-0.10(2)		0.12(2)		0.02(2)		-0.02(2)	0.11(2)	-0.04(2)	-0.07(2)		-0.04(2)	

Conclusion

The charge density study of estrone has proven be a fruitful start to our study. The information obtained from this study, while interesting by itself, is only a small part of what we need to reach our goal. Comparisons among the estrogen derivatives is what will give us the clues to how these molecules interact with the active site of the estrogen receptor. Analyzing such details as the electrostatic potential and using this information in conjunction with binding affinity and response studies, will help us better understand which regions of the molecules are responsible for the responses observed. Then, perhaps, better solutions can be found to fight breast cancer.

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Supplementary Material

Table S1. Coordinates and U_{iso}/U_{equ}

Atom	x	y	z	U_{iso}/U_{equ}, Å^2
O(1)	-1.34680(5)	-0.80603(4)	-0.31136(2)	0.021
O(2)	-0.81875(4)	-0.28620(3)	0.15646(2)	0.020
C(1)	-1.27682(6)	-0.55421(5)	-0.16808(2)	0.015
C(2)	-1.35934(6)	-0.62542(5)	-0.22325(2)	0.016
C(3)	-1.27227(6)	-0.73028(4)	-0.25802(2)	0.015
C(4)	-1.10335(6)	-0.76059(5)	-0.23765(2)	0.016
C(5)	-1.02037(6)	-0.68878(4)	-0.18216(2)	0.014
C(6)	-0.83713(6)	-0.72811(5)	-0.16262(3)	0.016
C(7)	-0.74628(6)	-0.62147(5)	-0.11658(3)	0.016
C(8)	-0.86423(5)	-0.57939(4)	-0.05414(2)	0.013
C(9)	-1.02098(6)	-0.50323(5)	-0.08570(2)	0.013
C(10)	-1.10811(6)	-0.58429(4)	-0.14583(2)	0.013
C(11)	-1.14593(6)	-0.45825(5)	-0.02538(2)	0.018
C(12)	-1.05677(6)	-0.37607(5)	0.03509(3)	0.018
C(13)	-0.90214(6)	-0.45319(4)	0.06484(2)	0.013
C(14)	-0.77798(6)	-0.48937(4)	0.00222(2)	0.013
C(15)	-0.61262(6)	-0.53501(5)	0.04127(3)	0.019
C(16)	-0.59946(6)	-0.43581(5)	0.10583(3)	0.019
C(17)	-0.78060(6)	-0.37820(5)	0.11507(2)	0.015
C(18)	-0.96034(7)	-0.57644(5)	0.10966(3)	0.021
H(1A)	-1.4620(10)	-0.7747(8)	-0.3220(4)	0.013
H(1)	-1.3465(8)	-0.4746(6)	-0.1415(3)	0.015

H(2)	-1.4901(9)	-0.6011(7)	-0.2378(4)	0.019
H(4)	-1.0363(9)	-0.8405(7)	-0.2652(4)	0.012
H(6A)	-0.8401(9)	-0.8210(7)	-0.1310(4)	0.015
H(6B)	-0.7663(9)	-0.7495(7)	-0.2125(3)	0.012
H(7A)	-0.6234(8)	-0.6583(6)	-0.0957(3)	0.014
H(7B)	-0.7185(8)	-0.5357(6)	-0.1517(3)	0.013
H(8)	-0.9134(8)	-0.6717(6)	-0.0288(3)	0.013
H(9)	-0.9627(7)	-0.4119(6)	-0.1085(3)	0.014
H(11A)	-1.2087(8)	-0.5462(6)	-0.0018(3)	0.011
H(11B)	-1.2436(8)	-0.3923(6)	-0.0488(3)	0.014
H(12A)	-1.1508(8)	-0.3525(7)	0.0773(3)	0.028
H(12B)	-1.0113(8)	-0.2803(6)	0.0135(3)	0.021
H(14)	-0.7432(8)	-0.3937(6)	-0.0238(3)	0.014
H(15A)	-0.6276(8)	-0.6385(7)	0.0611(3)	0.013
H(15B)	-0.5019(10)	-0.5250(7)	0.0044(4)	0.026
H(16A)	-0.5652(9)	-0.4839(7)	0.1572(4)	0.027
H(16B)	-0.5108(8)	-0.3531(6)	0.0948(3)	0.019
H(18A)	-1.0367(8)	-0.6424(6)	0.0780(3)	0.012
H(18B)	-1.0399(9)	-0.5319(7)	0.1497(4)	0.026
H(18C)	-0.8553(9)	-0.6325(7)	0.1304(4)	0.030

Table S2. Anisotropic Thermal Parameters U_{ij}, $Å^2$

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(1)	0.0241(2)	0.0210(2)	0.0175(2)	0.0039(1)	-0.0050(1)	-0.0054(1)
O(2)	0.0203(2)	0.0191(2)	0.0192(2)	-0.0001(1)	-0.0007(1)	-0.0038(1)
C(1)	0.0146(2)	0.0163(2)	0.0155(2)	0.0044(2)	-0.0023(1)	-0.0026(1)
C(2)	0.0164(2)	0.0170(2)	0.0148(2)	0.0032(2)	-0.0023(2)	-0.0022(2)
C(3)	0.0186(2)	0.0157(2)	0.0118(2)	0.0015(2)	-0.0008(2)	-0.0010(1)
C(4)	0.0176(2)	0.0161(2)	0.0132(2)	0.0034(2)	-0.0003(2)	-0.0010(1)
C(5)	0.0147(2)	0.0144(2)	0.0120(2)	0.0027(1)	0.0011(1)	0.0002(1)
C(6)	0.0147(2)	0.0164(2)	0.0169(2)	0.0039(2)	0.0020(2)	-0.0010(2)
C(7)	0.0129(2)	0.0162(2)	0.0184(2)	0.0018(2)	0.0037(2)	0.0003(2)
C(8)	0.0115(2)	0.0122(2)	0.0145(2)	0.0008(1)	0.0010(1)	0.0013(1)
C(9)	0.0133(2)	0.0132(2)	0.0133(2)	0.0028(1)	-0.0001(1)	0.0000(1)
C(10)	0.0134(2)	0.0136(2)	0.0133(2)	0.0033(1)	-0.0003(1)	-0.0005(1)
C(11)	0.0128(2)	0.0246(2)	0.0157(2)	0.0053(2)	-0.0013(2)	-0.0049(2)
C(12)	0.0160(2)	0.0209(2)	0.0170(2)	0.0064(2)	-0.0022(2)	-0.0044(2)
C(13)	0.0121(2)	0.0144(2)	0.0136(2)	-0.0004(1)	-0.0005(1)	0.0013(1)
C(14)	0.0116(2)	0.0134(2)	0.0153(2)	-0.0004(1)	0.0004(1)	0.0016(1)
C(15)	0.0129(2)	0.0220(2)	0.0229(2)	0.0036(2)	-0.0028(2)	-0.0026(2)
C(16)	0.0142(2)	0.0224(2)	0.0218(2)	-0.0001(2)	-0.0044(2)	-0.0013(2)
C(17)	0.0152(2)	0.0149(2)	0.0153(2)	-0.0009(2)	-0.0007(2)	0.0013(2)
C(18)	0.0238(2)	0.0210(2)	0.0167(2)	-0.0071(2)	0.0009(2)	0.0044(2)

Table S3. Bond Lengths

O(1) -	C(3)	1.3664(5)	C(8) -	H(8)	1.099(6)
O(1) -	H(1A)	0.967(8)	C(9) -	C(10)	1.5275(6)
O(2) -	C(17)	1.2274(5)	C(9) -	H(9)	1.099(6)
C(1) -	C(2)	1.3941(6)	C(11) -	H(11A)	1.092(6)
C(1) -	C(10)	1.4043(6)	C(11) -	H(11B)	1.092(6)
C(1) -	H(1)	1.077(6)	C(12) -	C(13)	1.5263(6)
C(2) -	C(3)	1.3985(6)	C(12) -	H(12A)	1.092(6)
C(2) -	H(2)	1.077(7)	C(12) -	H(12B)	1.092(6)
C(3) -	C(4)	1.3967(6)	C(13) -	C(17)	1.5172(6)
C(4) -	C(5)	1.4031(6)	C(14) -	C(15)	1.5396(6)
C(4) -	H(4)	1.077(6)	C(14) -	H(14)	1.099(6)
C(5) -	C(6)	1.5184(6)	C(15) -	H(15A)	1.099(6)
C(5) -	C(10)	1.4116(6)	C(15) -	H(15B)	1.099(7)
C(6) -	C(7)	1.5303(7)	C(16) -	C(17)	1.5279(6)
C(6) -	H(6A)	1.092(7)	C(16) -	H(16A)	1.092(6)
C(6) -	H(6B)	1.092(6)	C(16) -	H(16B)	1.092(6)
C(7) -	C(8)	1.5279(6)	C(18) -	H(18A)	1.059(6)
C(7) -	H(7A)	1.092(6)	C(18) -	H(18B)	1.059(7)
C(7) -	H(7B)	1.092(6)	C(18) -	H(18C)	1.059(7)
C(8) -	C(14)	1.5254(6)			

Table S4. Bond Angles

C(3)	O(1)	H(1A)	111.0(5)	C(14)	C(8)	H(8)	110.8(4)
C(2)	C(1)	C(10)	122.2(1)	C(10)	C(9)	H(9)	110.0(4)
C(2)	C(1)	H(1)	118.3(4)	C(1)	C(10)	C(5)	118.0(1)
C(10)	C(1)	H(1)	119.5(4)	C(1)	C(10)	C(9)	120.8(1)
C(1)	C(2)	C(3)	119.4(1)	C(5)	C(10)	C(9)	121.3(1)
C(1)	C(2)	H(2)	119.9(4)	H(11A)	C(11)	H(11B)	109.2(5)
C(3)	C(2)	H(2)	120.6(4)	C(13)	C(12)	H(12A)	112.2(4)
O(1)	C(3)	C(2)	122.4(1)	C(13)	C(12)	H(12B)	108.4(4)
O(1)	C(3)	C(4)	118.1(1)	H(12A)	C(12)	H(12B)	106.7(5)
C(2)	C(3)	C(4)	119.5(1)	C(12)	C(13)	C(17)	117.4(1)
C(3)	C(4)	C(5)	121.1(1)	C(8)	C(14)	C(15)	120.7(1)
C(3)	C(4)	H(4)	119.1(4)	C(8)	C(14)	H(14)	108.7(4)
C(5)	C(4)	H(4)	119.8(4)	C(15)	C(14)	H(14)	104.7(4)
C(4)	C(5)	C(6)	118.1(1)	C(14)	C(15)	H(15A)	110.1(4)
C(4)	C(5)	C(10)	119.9(1)	C(14)	C(15)	H(15B)	109.7(4)
C(6)	C(5)	C(10)	122.0(1)	H(15A)	C(15)	H(15B)	111.9(5)
C(5)	C(6)	C(7)	112.6(1)	C(17)	C(16)	H(16A)	107.0(4)
C(5)	C(6)	H(6A)	108.9(4)	C(17)	C(16)	H(16B)	108.5(4)
C(5)	C(6)	H(6B)	108.8(4)	H(16A)	C(16)	H(16B)	109.7(5)
C(7)	C(6)	H(6A)	107.6(4)	O(2)	C(17)	C(13)	126.5(1)
C(7)	C(6)	H(6B)	111.7(4)	O(2)	C(17)	C(16)	124.8(1)
H(6A)	C(6)	H(6B)	107.1(5)	C(13)	C(17)	C(16)	108.6(1)
C(6)	C(7)	C(8)	109.3(1)	H(18A)	C(18)	H(18B)	108.4(5)
C(6)	C(7)	H(7A)	111.4(4)	H(18A)	C(18)	H(18C)	107.6(5)
C(6)	C(7)	H(7B)	107.8(4)	H(18B)	C(18)	H(18C)	114.8(6)
C(8)	C(7)	H(7A)	110.5(4)				
C(8)	C(7)	H(7B)	110.4(4)				
H(7A)	C(7)	H(7B)	107.3(5)				
C(7)	C(8)	C(14)	114.2(1)				
C(7)	C(8)	H(8)	107.3(4)				

Table S5. Multipole Population Parameters for Hydrogen Atoms

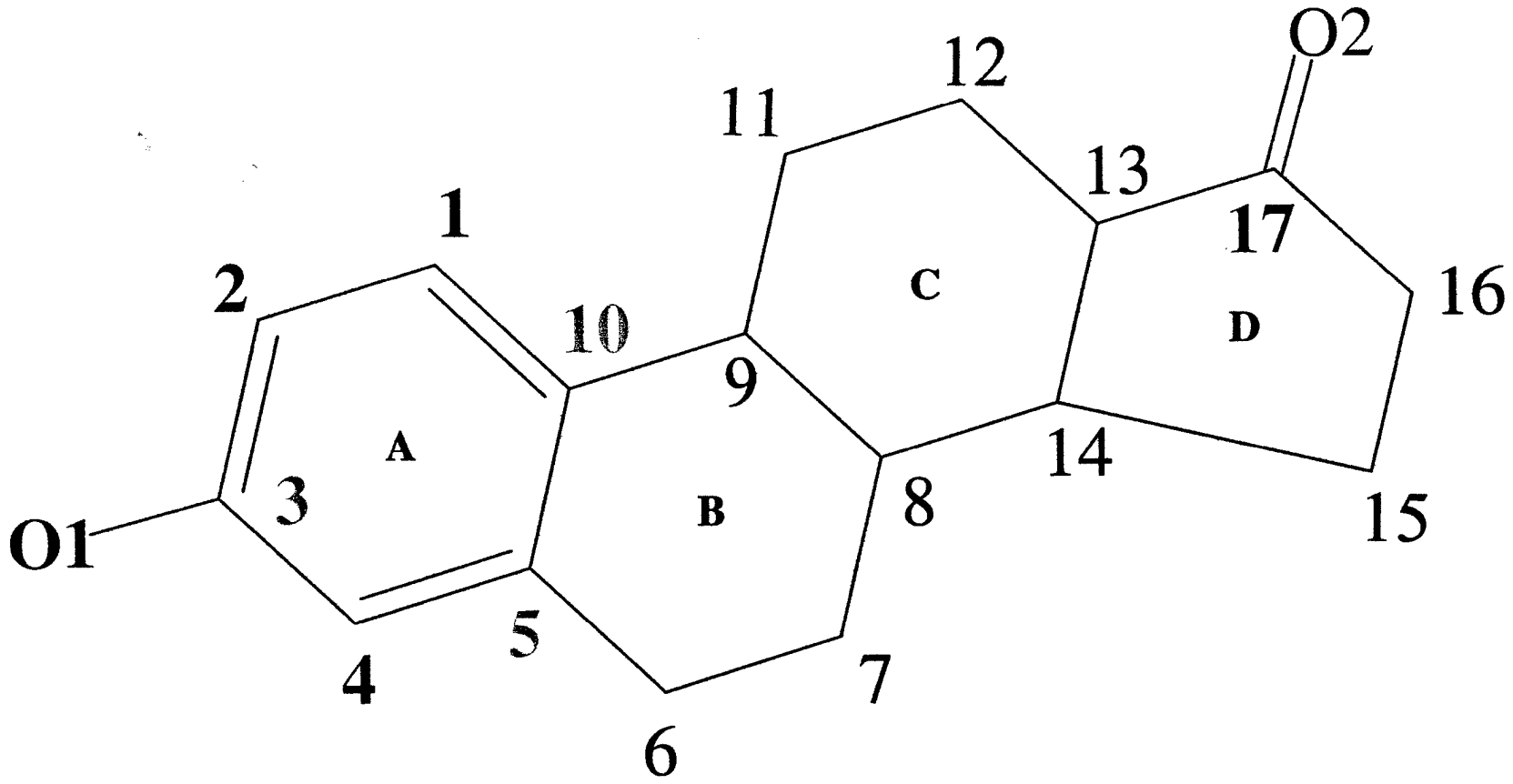
Atom	H(1A)	H(1)	H(2)	H(4)	H(6A)	H(6B)	H(7A)	H(7B)	H(8)	H(9)	H(11A)
κ'	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
D1+	0.10(1)	0.20(1)	0.21(1)	0.18(1)	0.190(7)	0.190(7)	0.156(8)	0.156(8)	0.12(1)	0.15(1)	0.097(8)

Atom	H(11B)	H(12A)	H(12B)	H(14)	H(15A)	H(15B)	H(16A)	H(16B)	H(18A)	H(18B)	H(18C)
κ'	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
D1+	0.097(8)	0.149(9)	0.149(9)	0.12(1)	0.15(1)	0.15(1)	0.198(8)	0.198(8)	0.140(7)	0.140(7)	0.140(7)

Table S6. Bond Critical Points

Bond	ρ	$\nabla^2\rho$	λ_1	λ_2	λ_3	R_{ij}	d_1	d_2
O(1)-C(3)	2.29(1)	-27.09(5)	-19.40	-17.54	9.85	1.367	0.837	0.530
O(2)-C(17)	2.90(1)	-7.59(7)	-27.48	-23.91	43.80	1.228	0.821	0.407
C(1)-C(2)	2.319(8)	-24.06(3)	-15.03	-14.71	5.68	1.395	0.702	0.693
C(1)-C(10)	2.32(1)	-25.74(3)	-16.63	-15.23	6.12	1.404	0.706	0.698
C(2)-C(3)	2.32(1)	-25.93(3)	-17.40	-14.74	6.21	1.399	0.738	0.661
C(3)-C(4)	2.34(1)	-24.62(4)	-17.09	-14.03	6.50	1.397	0.644	0.753
C(4)-C(5)	2.26(1)	-23.07(1)	-15.00	-13.77	5.70	1.404	0.628	0.776
C(5)-C(10)	2.17(1)	-21.01(4)	-14.94	-13.32	7.25	1.412	0.673	0.739
C(5)-C(6)	1.84(1)	-14.87(3)	-12.23	-11.34	8.70	1.518	0.772	0.746
C(6)-C(7)	1.695(8)	-11.08(2)	-10.61	-9.75	9.28	1.531	0.786	0.745
C(7)-C(8)	1.704(8)	-11.90(2)	-10.58	-10.12	8.80	1.528	0.801	0.727
C(8)-C(9)	1.688(9)	-11.64(3)	-10.85	-9.68	8.89	1.547	0.743	0.804
C(8)-C(14)	1.852(9)	-16.38(3)	-12.84	-11.96	8.43	1.526	0.780	0.746
C(9)-C(10)	1.76(1)	-15.18(3)	-11.85	-11.64	8.31	1.528	0.702	0.825
C(9)-C(11)	1.660(9)	-11.24(3)	-10.65	-9.73	9.14	1.541	0.753	0.788
C(11)-C(12)	1.672(9)	-11.25(3)	-10.50	-10.05	9.30	1.546	0.758	0.788
C(12)-C(13)	1.780(9)	-14.79(3)	-12.11	-11.19	8.51	1.528	0.792	0.736
C(13)-C(14)	1.70(1)	-13.63(3)	-11.03	-10.75	8.16	1.545	0.756	0.789
C(13)-C(17)	1.82(1)	-14.34(4)	-12.17	-11.49	9.32	1.518	0.780	0.738
C(13)-C(18)	1.722(9)	-14.30(3)	-11.64	-11.04	8.39	1.546	0.731	0.815
C(14)-C(15)	1.705(9)	-12.56(3)	-11.29	-10.26	8.99	1.540	0.767	0.773

C(15)-C(16)	1.667(9)	-10.27(3)	-10.23	-9.76	9.71	1.549	0.754	0.795
C(16)-C(17)	1.80(1)	-13.92(3)	-12.03	-11.72	9.88	1.528	0.766	0.762
O(1)-H(1A)	2.07(1)	-39.73(3)	-39.34	-38.20	37.81	0.967	0.806	0.161
C(1)-H(1)	1.844(6)	-18.39(2)	-16.35	-15.76	13.73	1.077	0.729	0.348
C(2)-H(2)	1.800(6)	-17.96(2)	-16.62	-14.76	13.42	1.077	0.730	0.347
C(4)-H(4)	1.736(7)	-17.83(2)	-15.99	-14.75	12.91	1.077	0.733	0.344
C(6)-H(6A)	1.713(7)	-18.26(2)	-15.99	-15.18	12.91	1.092	0.744	0.348
C(6)-H(6B)	1.682(8)	-16.91(2)	-15.19	-14.90	13.18	1.092	0.745	0.347
C(7)-H(7A)	1.726(8)	-16.49(2)	-15.72	-14.77	13.99	1.092	0.737	0.355
C(7)-H(7B)	1.723(7)	-16.00(2)	-15.61	-14.89	14.50	1.092	0.743	0.349
C(8)-H(8)	1.686(7)	-15.26(2)	-15.17	-14.63	14.54	1.099	0.745	0.354
C(9)-H(9)	1.746(8)	-15.42(3)	-15.08	-14.73	14.39	1.099	0.726	0.373
C(11)-H(11A)	1.682(7)	-13.85(2)	-14.93	-14.25	15.33	1.092	0.736	0.356
C(11)-H(11B)	1.613(7)	-11.24(2)	-14.34	-13.04	16.14	1.092	0.742	0.350
C(12)-H(12A)	1.779(8)	-15.47(3)	-16.39	-13.97	14.88	1.092	0.715	0.377
C(12)-H(12B)	1.725(8)	-12.49(3)	-14.54	-13.38	15.42	1.092	0.718	0.374
C(14)-H(14)	1.690(8)	-14.04(3)	-15.05	-13.75	14.76	1.099	0.734	0.365
C(15)-H(15A)	1.638(8)	-12.42(2)	-13.78	-13.53	14.88	1.099	0.739	0.360
C(15)-H(15B)	1.648(9)	-12.87(2)	-15.19	-13.46	15.78	1.099	0.752	0.347
C(16)-H(16A)	1.778(8)	-17.11(3)	-16.29	-14.88	14.07	1.092	0.728	0.364
C(16)-H(16B)	1.724(8)	-16.28(3)	-14.96	-14.63	13.31	1.092	0.715	0.377
C(18)-H(18A)	1.725(8)	-14.31(2)	-15.74	-13.94	15.36	1.059	0.708	0.351
C(18)-H(18B)	1.689(8)	-13.34(2)	-14.99	-14.12	15.78	1.059	0.714	0.345
C(18)-H(18C)	1.794(8)	-15.90(2)	-16.98	-14.30	15.38	1.059	0.711	0.348
H(1A)...O(2)	0.204(2)	3.143(2)	-1.33	-1.23	5.71	1.852	0.614	1.238



* All hydrogens atoms constrained as equivalent

Figure S1. Chemical Equivalents

Figure S2

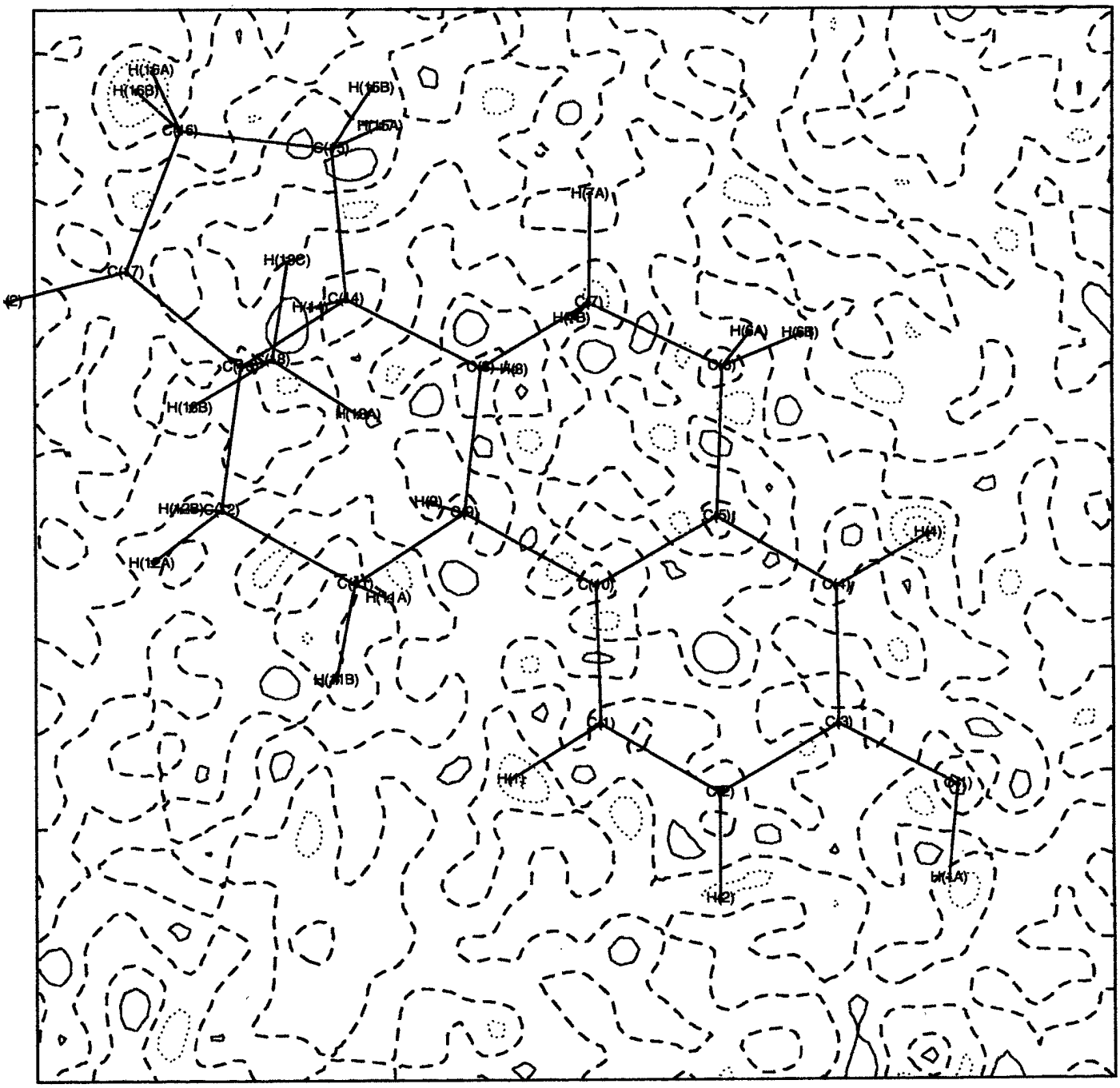

H(16A)
H(16B)
C(16)
H(15B)
H(15A)
C(15)
H(7A)
C(17)
H(13C)
C(14)
H(14)
C(7)
H(7B)
H(6A)
H(6B)
C(6)
C(13)
C(8)
H(8)
H(13B)
H(13A)
H(12B)
C(12)
H(9)
C(9)
C(5)
H(5)
H(12A)
C(10)
H(14A)
C(11)
C(4)
C(3)
H(11B)
H(1)
C(2)
C(1)
H(2)
H(3A)

Figure S3

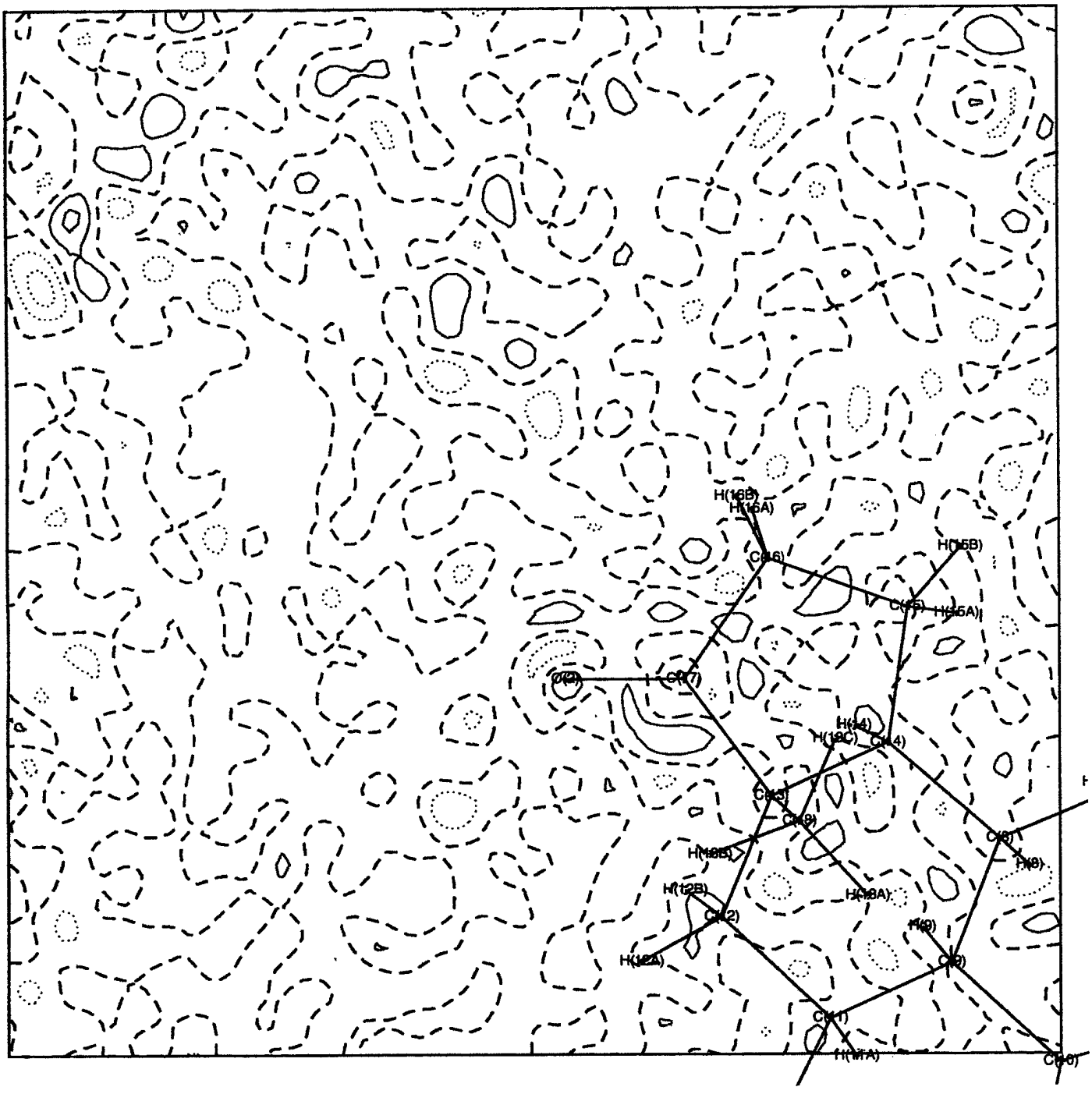

H(16B)
H(16A)
C(16)
H(15B)
C(15)
H(15A)
O(2)
C(7)
H(14)
H(19C)
C(14)
C(13)
C(9)
C(8)
H(8)
H(18B)
H(12B)
H(18A)
C(12)
H(9)
C(10)
H(12A)
C(11)
H(11A)
C(6)

Figure S4

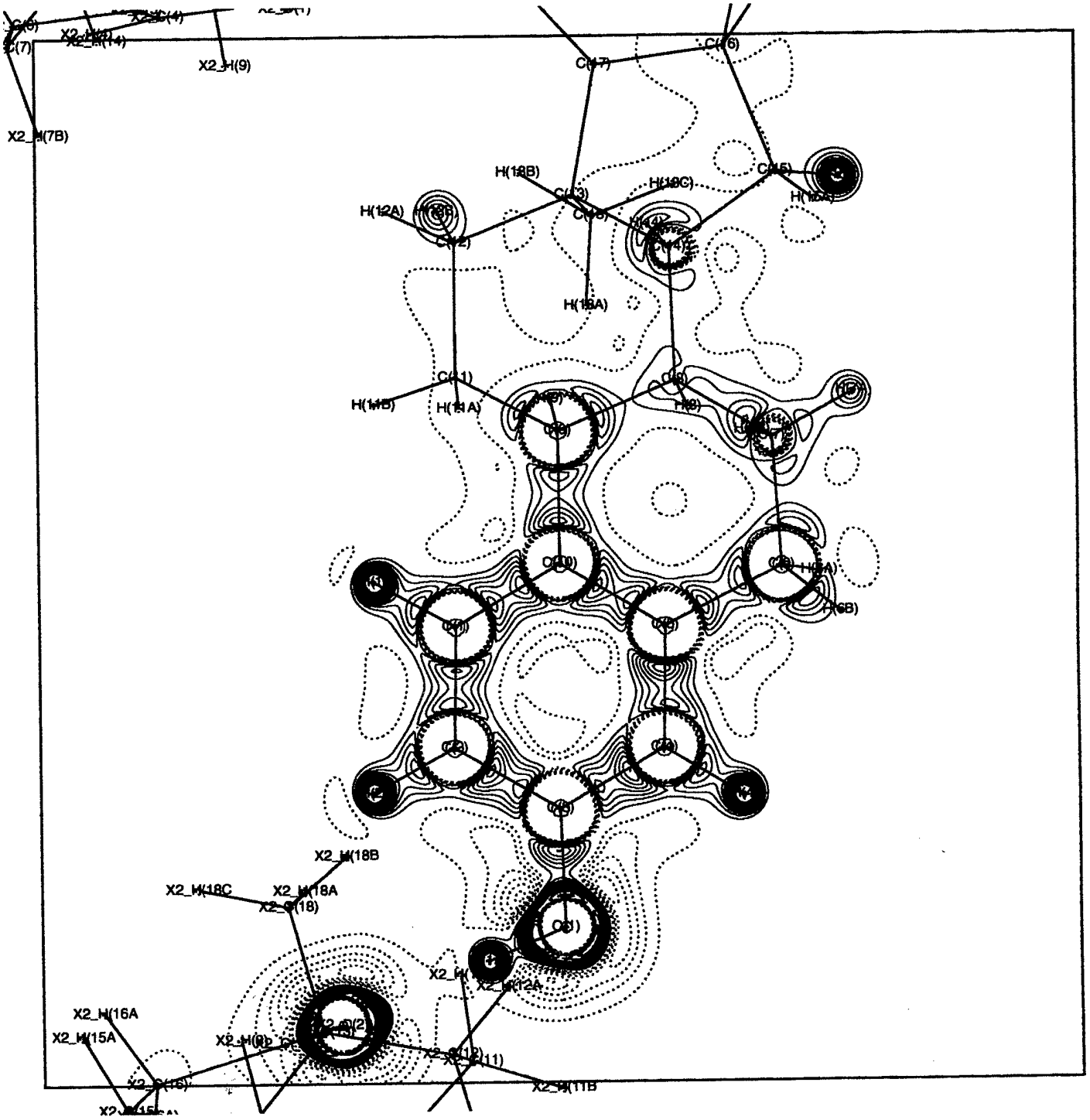
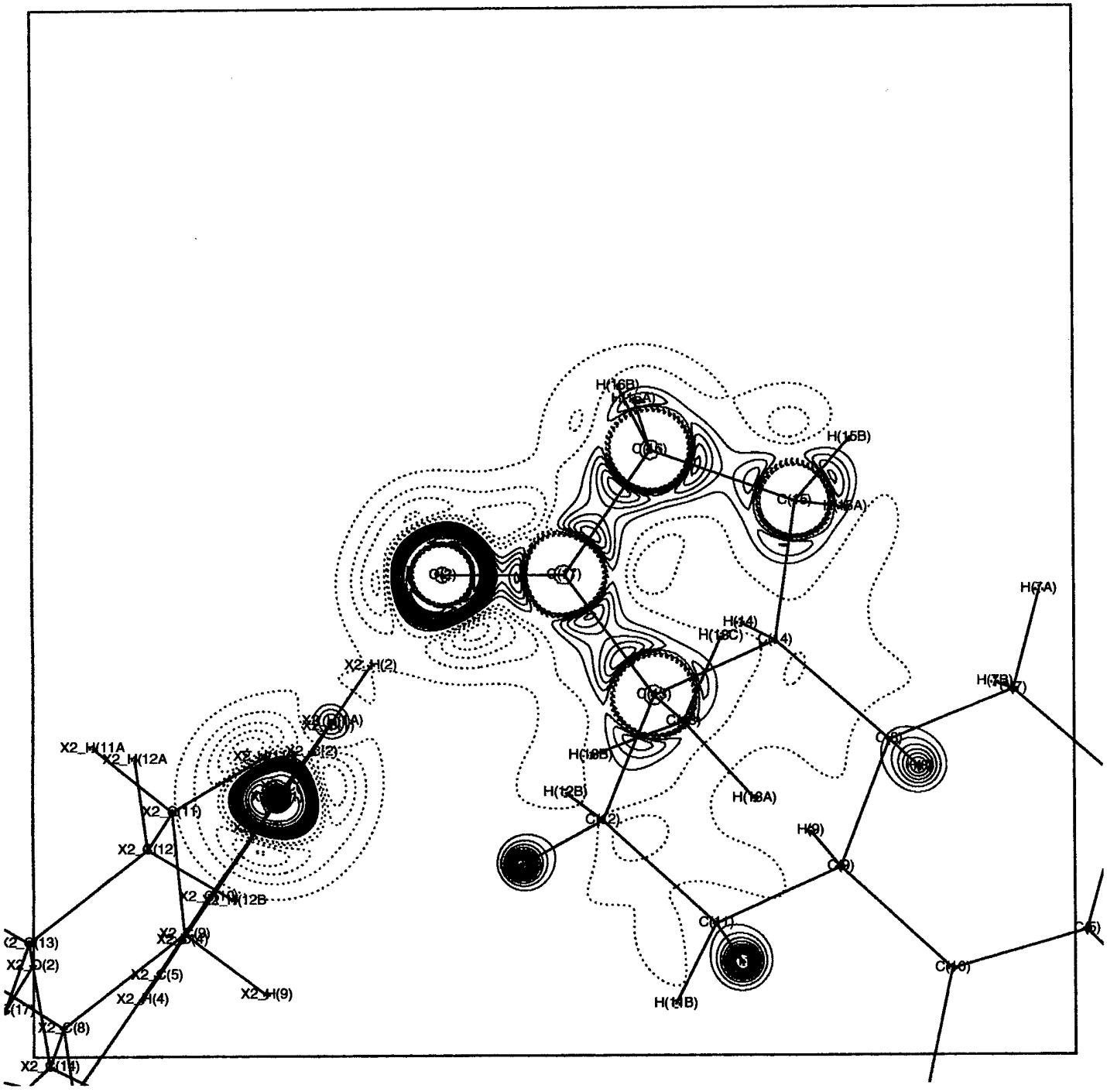

X2_H(9)
X2_H(7B)
H(18B)
H(18C)
H(12A)
H(18A)
H(11B)
X2_H(18B)
X2_H(18C)
X2_H(18A)
X2_H(16A)
X2_H(15A)

Figure S5


H(16B)
H(16A)
C(16)
H(15B)
C(15)
H(15A)
O(8)
C(7)
H(14)
H(13C)
C(14)
H(7A)
H(7B)
C(7)
X2_H(2)
C(13)
C(3)
H(18B)
H(18A)
C(18)
X2_H(11A)
X2_H(12A)
H(12B)
C(12)
H(9)
C(9)
X2_H(12B)
C(11)
C(6)
C(10)
X2_H(9)
X2_C(5)
X2_H(4)
X2_H(9)
X2_C(8)
H(14B)